THE MEDICAL JOURNAL OF AUSTRALIA

VOL. I.—15TH YEAR. SYDNEY, SATURDAY, FEBRUARY 11, 1928. No. 6.

Authors of articles submitted for publication are requested to read the following instructions and to comply with them.

All articles must be typed with double or treble spacing. Carbon copies should not be sent. Abbreviations should be avoided, especially those of a technical character at times employed in ward notes. Words and sentences should not be underlined or typed in capitals. The selection of the correct type is undertaken by the Editors. When illustrations are required, good photographic prints on glossy gaslight papers should be submitted. Each print should be enclosed in a sheet of paper. On this sheet of paper the number of the figure and the legend to appear below the print should be typed or legibly written. On no account should any mark be made on the back of the photographic print. If no good print is available, negatives may be submitted. Line drawings, graphs, charts and the like should be drawn on thick, white paper in India ink by a person accustomed to draw for reproduction. The drawings should be large and boldly executed and all figures, lettering and symbols should be of sufficient strength and size to remain clear after reduction. Skiagrams can be reproduced satisfactorily only if good prints or negatives are available. The reproduction of all illustrations but especially of skiagrams entails the sacrifice of time and energy and is expensive. Authors are expected to take a corresponding amount of trouble on the preparation of their illustrations, whether skiagrams, photographs, wash drawings or line drawings. The references to articles and books quoted must be accurate and should be compiled according to the following scheme. The order should correspond to the order of appearance in the article. The initials and surnames of the authors, the full title of the article or book, the full (unabbreviated) title of the journal in which the article appears, the date of the issue (day, month and year) and the number of the first page should be given in this sequence.

Table of Contents

[The Whole of the Literary Matter in THE MEDICAL JOURNAL OF AUSTRALIA is Copyright.]

ORIGINAL ARTICLES— PAGE

"Laboratory Diagnosis," by J. H. B. WALCH, M.B. 166
"The Present Position of Our Knowledge and Treatment of Preeclampsia and Eclampsia," by CECIL COGHLAN, M.B., Ch.M., F.R.C.S., M.R.C.P.I., D.G.O., L.M. 170
"Vascular Disturbances as an Explanation of Nervous Symptoms," by ARTHUR E. MILLS, M.B. 176

REPORTS OF CASES—

"Resection and Anastomosis for Intussusception in an Infant," by R. H. MACDONALD, M.B., Ch.M. 182

REVIEWS—

A Beginner's Guide to Practice 183
The Value of Vaccination 184

LEADING ARTICLES—

A Retrospect 185

CURRENT COMMENT—

The Prevention of Diphtheria 187

ABSTRACTS FROM CURRENT MEDICAL LITERATURE—

Physiology 190
Biological Chemistry 191

BRITISH MEDICAL ASSOCIATION NEWS— PAGE.

Scientific 192
Nominations and Elections 193

POST-GRADUATE WORK—

Lectures at Launceston 193
Oto-Rhino-Laryngology 193
Lectures in Melbourne 193

RESEARCH—

Science Scholarships and Grants 194

CORRESPONDENCE—

Workers' Compensation Act 194
Red-backed Spider Bite 194
Press Notices 195
Post-graduate Work in Paris 195

PROCEEDINGS OF THE AUSTRALIAN MEDICAL BOARDS—

Victoria 195

MEDICAL APPOINTMENTS 195
BOOKS RECEIVED 195
DIARY FOR THE MONTH 196
MEDICAL APPOINTMENTS VACANT, ETC. 196
MEDICAL APPOINTMENTS: IMPORTANT NOTICE 196
EDITORIAL NOTICES 196

LABORATORY DIAGNOSIS.[1]

By J. H. B. WALCH, M.B.,
Hobart, Tasmania.

MY original idea for this paper was to discuss in general terms the value of laboratory tests to the practitioner; but, on thinking it over, I decided it would be more useful to deal rather with the advantages and limitations of the various tests available for the diagnosis of particular diseases. I propose to discuss the ordinary tests used to assist in the diagnosis of three common conditions, reminding you of facts concerning their use and interpretation. You have probably all heard this before, but may be apt to forget.

Syphilis.

I start with syphilis. The first test available is the examination of smears from a suspected lesion. The treponema is invariably present in the primary sore and nearly always in sufficiently large numbers to be easily demonstrated. In secondary lesions the numbers are not so great, but the organisms can often be found, while in tertiary lesions they can seldom be demonstrated by ordinary methods. It follows then, that a failure to find treponemata on an examination of suitable material from a primary sore is of considerable value. The value of a positive result depends, of course, on the satisfactory identification of the microbe. There are other organisms which, although not absolutely the same, resemble *Treponema pallidum* so closely that most observers cannot distinguish them by observation alone. Such organisms occur in the mouth, but are not found on the genital organs and never invade the tissues. On the surface of an ulcerated chancre other spirochætes are often present, but these are fairly easily distinguished from the specific treponema. The value of a positive finding, then, depends largely on the careful collection of material from the depth of a lesion, without contamination from the surface. The method of obtaining the material is as follows: Wash the lesion with alcohol, dry and rub with gauze or scrape gently with a scalpel. Then wait a few minutes till lymph exudes from the deeper layers. Avoid bleeding if possible; but should it occur, wipe the blood gently away and wait till clear lymph exudes. Thin smears may be made at once or the lymph may be collected in a capillary pipette or Wright's blood tube. For dark field examination dry smears are useless and if the material is collected on a slide it must be covered with a slip at once and examined within a few minutes.

As regards the methods of examination the dark field is useful where a quick result is required. Its principal use is in the out patients' department of a hospital or a doctor's own rooms, where a certain diagnosis may be made in a few minutes. As a laboratory test the silver impregnation methods are much better, since the organism can be demonstrated with certainty and examined more satisfactorily and its spirals can be counted and measured. Staining methods are satisfactory, if carefully carried out, but more apt to go wrong, so that one may be uncertain whether the organisms have not escaped unstained. The same may be said of the Indian ink method.

The next test for syphilis is the complement deviation or Wassermann test. This is not the place for a discussion of the theory and technique of the test; but some brief observations are necessary to assist an explanation of the method of reporting and interpreting the result.

In 1901 Bordet and Gengou, working with bacteria, devised the mechanism of the complement deviation test. In 1906 Wassermann and Bruck attempted to adapt the test to the diagnosis of syphilis. Being unable to cultivate the treponema, they used as an antigen an extract of congenital syphilitic liver which contained the organisms in very large numbers. They developed a reliable test for syphilis. Later Marie and Levaditi showed that normal liver extract acted just as well as the syphilitic liver extract and even that comparatively simple lipoids such as lecithin and cholesterol can be used for the antigen. This amazing discovery exploded a bombshell among the theories of the immunologists. The Wassermann test was devised as the first practical application of an established theory. Its success seemed to confirm the idea from which it originated and then it was found that the reaction which actually takes place is not that which was anticipated. The success depends on an accidental detail of the original technique and its value depends entirely on statistical evidence.

In the early investigations it was soon recognized that the reaction is quantitative. The amount of the reacting substance in different sera varies, some react strongly, others feebly. Various methods were devised for estimating the strength of the reaction and it became customary to indicate the result by *plus* and *minus* signs, so that a "+ + +" reaction was strongly positive and a "+" feebly positive.

Unfortunately, owing to the diverse methods employed the reports from different investigators did not always agree. There are still different methods used, but that elaborated by Colonel L. W. Harrison and recommended by the Medical Research Council, is becoming the standard technique. It is used in the big hospitals in Melbourne and Sydney and it is the method I employ here. The strength of the reaction is measured by the number of minimum hæmolytic doses of complement deviated. A strongly positive result may be due to the deviation of eight to twenty minimum hæmolytic doses, while deviation of four of five minimum hæmolytic doses would be a feebly positive result. It is regrettable that many workers continue to use the old *plus* method of reporting, when a definite numerical value can be substituted for it. In my reports I give the number of minimum hæmolytic doses of complement deviated and also the verbal equivalent, strongly positive, positive, feebly positive or "negative." The numerical value allows of accurate comparisons between different tests, so long as the

[1] Read at a meeting of the Tasmanian Branch of the British Medical Association on December 13, 1927.

same technique is used. Of course, such numbers would be meaningless without strict adherence to the standard procedure. The sensitiveness of the reaction can be varied by modifying the reagents and the method of incubation, so that a serum which deviates six minimum hæmolytic doses by the standard technique might be made to deviate eight minimum hæmolytic doses by changing the antigen and using the ice-box method. The standard technique is intended to give a safe and reliable test, not so sensitive as to risk getting false positive results. Sometimes, greater sensitiveness is desirable as a guide to treatment or a test of cure. Then the ice-box method should be used.

With regard to interpretation of results, a strongly positive result with a properly performed test is obtained only in syphilis and yaws. A feebly positive result is presumptive evidence of syphilis, but not conclusive. Various observers have claimed that reactions may be obtained in leprosy, trypanosomiasis, relapsing fever, tropical ulcer, malaria at the height of the fever, scarlet fever for a short period and acute miliary tuberculosis. Failure to obtain a reaction can never absolutely exclude syphilis, even in untreated cases. If antisyphilitic treatment has recently been administered failure to secure a reaction has no value whatever, but in untreated cases in certain stages the evidence afforded by absence of reaction is very weighty. Where the diagnosis rests between early secondary syphilis and some other disease, in the absence of treatment a failure to react, especially if repeated once or twice, would be almost conclusive against syphilis. In other stages the value of a failure to react is not so great.[1]

Summarizing the results obtained by serologists in different parts of the world, the figures in untreated cases are as follows:[2]

In primary syphilis 69·8% of sera yield a reaction.

In secondary syphilis 89·4% of sera yield a reaction.

In tertiary syphilis 78·1% of sera yield a reaction.

In hereditary syphilis 94·5% of sera yield a reaction.

In cerebro-spinal syphilis 47·6% of sera yield a reaction.

In general paralysis 88·1% of sera yield a reaction.

In tabes 62·6% of sera yield a reaction.

Taking cerebro-spinal fluid instead of serum general paralysis gives 90% of reactions, tabes gives 56·2% and cerebro-spinal syphilis only 19%.

The reaction generally appears first from the fifteenth to the thirtieth day after infection, about the time when there is definite infiltration of the chancre, but it may be delayed. During the secondary stage the reaction becomes progressively stronger. In the tertiary period the reaction usually continues to be strong as long as the disease is active, but if the infection becomes latent, the reaction weakens and may disappear, recurring when symptoms recur. Sometimes a definite gumma may appear while the Wassermann test yields no reaction. In congenital syphilis the result of the test is usually strongly positive at birth, but often dies away about puberty.

With regard to the effect of treatment, mercury is most important, as it rapidly changes the power of the serum to react. This power may be revived after the treatment is stopped. The effect of "Salvarsan" is first to increase the reaction and then gradually to remove it, but here again it may recur. When taking blood for a progress test, all treatment should have been stopped for at least a fortnight and preferably a month. When making the final test for cure, there should have been no treatment for six months, unless a provocative dose of "Salvarsan" be given ten days before the blood is taken.

In about 6% of early cases and 22% of late ones the reaction remains in spite of all treatment.[3]

It occasionally happens that a patient's serum will destroy complement, even in the absence of antigen. In such cases the serum is said to be anticomplementary and the test is worthless. In my experience the condition is usually of short duration and a satisfactory test may be obtained after an interval of a few weeks.

There are a few points to mention with regard to the collection of specimens. The quantity of blood should be at least five cubic centimetres. There should be no difficulty in obtaining this from an ordinary adult patient, though with young children and very fat people trouble may be encountered. I think some people have trouble through not using a wide enough needle to puncture the vein. The needles used for injections are not usually large enough to allow free passage to blood.

Many specimens are spoilt by laking of the corpuscles, caused by the presence of water in the syringe, needle or container. A very small quantity of water is sufficient to make the test impossible.

The blood should not be kept more than twenty-four hours before the test is done. A serum loses its power to react fairly rapidly. Of course serum which gives a strong reaction will give a reaction after quite a long period, but the more feeble reactions are apt to be lost with delay.

The flocculation tests for syphilis, particularly the Kahn test, are increasing in popularity. These probably depend on the same fundamental reaction as the Wassermann, but the method of demonstrating them is quite different, depending on the formation of a precipitate instead of the deviation of complement. The actual test is much simpler to perform than the Wassermann, but the preliminary work involved in the preparation of the antigen is rather critical. The Kahn test has recently been adopted as the standard for the United States Naval Medical Services in place of the Wassermann test. In over fifty-six thousand cases by various workers the results of the two tests agree in about 90%.[4] The precipitation test is rather less sensitive than the Wassermann. It can be used with anticomplementary sera, but not with cerebro-spinal fluid.

With regard to the examination of cerebro-spinal fluid in syphilis, I have mentioned the results to be expected with the Wassermann test. The globulin test and cell count give useful information, but are not conclusive. The colloidal gold test is of great value. It depends on the precipitation of gold

from colloidal solution by pathological fluids. Eleven test tubes are used, containing the colloidal gold with progressive dilutions of cerebro-spinal fluid from one in ten to one in ten thousand two hundred and forty. Precipitation occurs at different dilutions with three types of case. In the paretic response it is between one in ten and one in six hundred and forty. In the luetic reaction the maximum reduction occurs between one in forty and one in eighty, while the meningitic response is mainly between one in three hundred and twenty and one in six hundred and forty.

The result is usually expressed by a numerical scheme, in which nought represents the absence of precipitation, five stands for complete precipitation and two, three and four for intermediate degrees recognized by the change in colour. The figures are given for each of the eleven tubes in order, so that the paretic response becomes 5555 4 33 1 000, the luetic response is 00 2 4 3 11 0000 and the meningitic response 0000 1 3 44 3 00. In general paralysis a paretic response is said to be obtained in every case.[5] The luetic response obtained in tabes and cerebro-spinal syphilis is of somewhat less value. The meningitic response is not much use at all. It is obtained when there are traces of blood in the fluid and in meningitis probably depends on the leakage of blood protein. On the whole the results agree closely with the cerebro-spinal Wassermann, though the colloidal test is of more value in general paralysis.

The various other colloidal tests, such as the mastic, Berlin blue, benzoin, gamboge and collargol reactions are not so reliable.

Gonorrhœa.

I pass on now to the tests for gonorrhœa. The first is the examination of a stained smear from the urethra, vagina or cervix. You are familiar with the appearance of the classical gonococcal smear. The typical kidney shaped organisms grouped within polymorphonuclear leucocytes present an unmistakable picture which is duplicated only in smears from cerebro-spinal meningitis. When this classical picture is obtained in smears from the uro-genital tract, the diagnosis of gonorrhœa is complete and certain, but unfortunately in practice such a picture is the exception rather than the rule. It is found fairly often in recent uncomplicated infections of the male urethra and less often in the female. Sometimes a smear shows a large number of polymorphonuclear leucocytes, but no bacteria of any sort. These infections are nearly always gonococcal, but it may be impossible to clinch the diagnosis. Cultures are more likely to be successful than smear examinations. The usual picture, especially in old infections and in the female, shows a field swarming with different kinds of bacteria, both intra- and extracellular, with or without diplococci resembling gonococci. Concerning these smears I quote from David Thomson's book on gonorrhœa.[6] He writes:

> The majority of such smears when examined by the microscope show myriads of organisms, diplococci and diplobacilli, Gram positive and Gram negative and only a bold and inexperienced observer would dare to diagnose the presence of isolated gonococci in such a mass of bacteria. The diagnosis is only certain where numbers of gonococci are found intracellularly.

In the majority of chronic infections in females smears apparently contain no gonococci or are doubtful. Cultures give similar results. From a practical standpoint all such infections should be regarded as of gonococcal origin until proved otherwise.

Another type of finding is common in old-standing gleet. Here the discharge may consist largely of epithelial cells, with perhaps about 50% of polymorphonuclear leucocytes. Gonococci are so scarce that they are difficult to detect. All efforts to find them by microscopical and cultural examinations of even urine deposits, shreds and expressed prostatic secretion may entirely fail, yet a true relapse may often occur, when gonococci again become apparent.

There may be found in smears a number of other diplococci resembling the gonococcus, some closely, others but slightly. These never present a picture like the classical gonorrhœa smear, but in a mixed infection it is often quite impossible even to form an opinion as to whether certain organisms are gonococci or not. There is a small Gram negative bacillus, somewhat resembling the *Bacillus influenzæ*, which is found in about 2·6% of chronic infections in the male and about 36% in the female. This organism is very variable in shape and the shorter forms are apt to be mistaken for gonococci. Generally speaking the smear diagnosis of chronic gonorrhœa, especially in women, is very difficult and unsatisfactory. The examination of vaginal smears is almost without value in adults. It is much more important to examine pus expressed from the urethra or pus from the cervix or cervical canal.

Provocation by chemical irritants is a procedure which is often useful when no gonococci can be found by direct examination, not so much for establishing diagnosis in the first instance as in determining whether a chronic discharge is still infective. The method consists in giving one injection of a chemical irritant, usually silver nitrate and making smears next day. By this means deeply situated gonococci may be dislodged and, further, the hyperæmia and serous infiltration are conducive to the multiplication of the germs.

Cultural methods for the diagnosis of gonorrhœa are being much more employed now than formerly, but they are by no means perfect. The difficulties are three, preparing a suitable medium for the growth of the gonococcus, obtaining viable germs for implantation and isolating the gonococcal colonies from the more exuberant growth of the numerous other germs often present. The question of the medium has been satisfactorily settled. There are several suitable formulæ available; but Thomson's human blood-phosphate-agar is probably the best.

The difficulty of obtaining viable gonococci is rather serious in chronic cases. Probably the great majority of the diplococci present in the discharge are already dead. It is advisable to dislodge those

embedded in the mucous membrane by rubbing fairly hard with a sterile swab.

The isolation of the germs is attempted by spreading the material over a large surface of medium in several plates, but where the secondary infection is heavy and the gonococci few, there is not much chance of separating them.

Cultural methods, then, are valuable chiefly in two circumstances. Where there is an apparently sterile secretion, cultures are more likely to reveal the organism than smear examinations. Secondly, where diplococci are present alone or with few other organisms, but cannot be identified with certainty in the smear, they may be cultivated and subjected to fermentation tests. In the chronic cases with a heavy secondary infection it may be worth attempting cultivation to identify the gonococcus, but the chance of success is small. Under no circumstances can a cultural examination yielding no result be taken as completely excluding gonorrhœa.

The complement deviation test for gonorrhœa has given very valuable results in the hands of many investigators, but at its present stage of development it is rather critical. While a positive response to the Wassermann test involves the deviation of say eight minimum hæmolytic doses of complement, a gonorrhœal serum yielding a strong reaction would deviate only three, so that it is necessary for the reaction to be carried out with extreme care and with very full controls.

Nevertheless, it is useful in some cases, particularly in systemic or joint infections and in old infections of doubtful origin. The reaction may usually be obtained about a fortnight after the appearance of the discharge and it remains for about three months after the gonococci have disappeared. The more extensive the inflammation, the greater the probability of a positive result. Mild infections are likely to yield no reaction throughout. It is probable that a more sensitive antigen may be evolved before long and more reliable results obtained.

Other tests which have been used with success are the provocative dose of vaccine, the cutireaction and the precipitin test. In each case good results have been claimed, but they have proved rather variable with different workers and the tests have not come into general use.

Before passing on I shall deal briefly with non-gonococcal urethritis. Although the vast majority of purulent discharges from the urethra are gonococcal in origin, there can be no doubt that a urethritis may be primarily due to other organisms, usually staphylococci or diphtheroid bacilli. There is nearly always some preceding damage to the mucous membrane. The majority of cases occur in those who have had gonorrhœa and in whom the membrane remains delicate and susceptible to attack by common pyogenic organisms. Another common cause is the use of an iritating injection, usually a precautionary measure on the part of the patient. Mechanical iritation may have the same result and one must always remember the possibility of an intraurethral chancre.

Primary urethritis occasionally follows certain systemic diseases, as enteric fever, measles and influenza.

As a general rule non-gonococcal infections are not transmissable in the ordinary way, but there are a number of recorded cases in which they have been undoubtedly passed on.

I would emphatically advise that every case of purulent urethritis be regarded as gonorrhœa as far as treatment and the risk of transmission are concerned. The only exceptions which must be watched for are the cases of chemical irritation; these would be aggravated by vigorous treatment.

Diabetes.

The third condition I propose to discuss is diabetes. Testing the urine is a routine measure with most practitioners and it is nearly always done in an improper manner. In the first place Fehling's solution is usually employed and it gives a most misleading and inaccurate result both qualitatively and quantitatively.[7] The reagent is reduced by uric acid, creatinin, glycuronic acid, lactose, pentose and homogentisic acid, as well as by glucose. On the other hand small quantities of glucose may be destroyed by the heating with strong alkali. Hence a reaction to Fehling's test does not necessarily mean that the patient has glycosuria; nor does no reaction exclude the presence of traces of glucose. When the test is done with equal quantities of reagent and urine, nothing less than a very definite, bright yellow precipitate can be regarded as evidence of the presence of sugar and even in such a case one cannot assume that the sugar is glucose.

Benedict's reagent is much better. It is, of course, reduced by lactose and pentose as well as by glucose, but not by uric acid or creatinin. It should always be used in the standard manner, eight drops of urine being added to five cubic centimetres of reagent and the mixture boiled for two minutes and allowed to cool. With such a test even an opalescent green colour is definite evidence of the presence of a reducing sugar.

There are several tests available for determining which variety of sugar is present in urine.

The phenylhydrazone test is usually the most convenient and it gives a quite definite distinction, but it fails when only a trace of sugar is present. About 0·5% of lactose or rather less glucose must be present to be sure of obtaining a result, though in some cases a smaller quantity may suffice.

The polarimeter method can be used with smaller proportions of sugar, but requires special apparatus and is subject to fallacies due to the presence of other optically active substances.

The fermentation test is accurate, if carefully controlled, but there must always be positive and negative controls, since samples of yeast vary greatly in their ability to ferment sugars. It is not more delicate than the phenylhydrazone test.

I would like to impress you with the importance of remembering the probability of lactose being found in the urine of pregnant or lactating women. Small quantities occur quite frequently and some-

times a considerable amount. This is especially likely to happen when a mother has to give up nursing while there is still a plentiful supply of milk. The condition, of course, can be recognized easily if the amount of sugar is sufficient to give the distinguishing test, but when only a trace is present, it may be difficult to distinguish from mild diabetes, especially as a little lactose may be present in the blood also, giving a slightly raised blood sugar content.

The quantitative estimation of sugar in urine may be performed by a number of methods which I need not describe, but I shall remind you of the necessity for taking the sample from the mixed twenty-four hours urine and having the estimation performed without delay. Sugar will gradually disappear even from a sterile sample and in heavily infected urine, that is in the usual sample, it will be destroyed with great rapidity. When sugar is found, aceto-acetic acid should always be looked for. Gerhardt's test with ferric chloride should not be used. It is not sufficiently sensitive, is subject to fallacies and does not reveal the presence of acetone, to which diacetic acid is converted on standing. If a true reaction is obtained with this test immediate and drastic steps must be taken in the treatment, since a dangerous degree of ketosis is present. False reactions are given by any phenyl compound, for instance if the patient has been taking aspirin or any of the salicylate derivatives. The best test for the acetone bodies is Rothera's nitroprusside reaction. It is extremely delicate, there are no fallacies and it is given by acetone as well as aceto-acetic acid. The depth of colour gives a very good indication of the amount of the acetone bodies present.

The blood sugar estimation is by far the most important test for diabetes. There are many methods of performing it, most of them involving a colourimetric comparison with standard solutions. I use the technique of Folin and Wu which requires about one cubic centimetre of oxalate blood. The blood does not have to be accurately measured at the time of collection, but merely drawn off with a syringe, put at once into a bottle with a suitable quantity of powdered potassium oxalate and well shaken. About two milligrammes of oxalate are required for one cubic centimetre of blood. The exact proportion is not important, but there should not be a large excess. It is advisable to take more than one cubic centimetre of blood where convenient, to allow for loss in manipulation. There is a modification of this method in which the blood is collected from a needle prick in a special pipette like that used for cell counts. Only 0·16 cubic centimetre of blood is required in this case, but the special pipette must be used.

It is no use doing blood sugar estimations at random without regard to the carbohydrate intake. The best results from a single test are obtained by taking the blood two hours after giving fifty grammes of glucose in four hundred cubic centimetres of water. By this means the maximum difference is obtained between the results in normal persons, diabetes and renal glycosuria. When a complete study of a case is required, the first specimen should be taken in the morning with the patient starving from the night before. Then the fifty grammes of glucose should be given and samples of blood collected at half-hourly intervals for two hours. This procedure gives a very clear idea of the condition, but is only necessary for diagnosis in a few doubtful cases. The estimation after glucose is given provides a definite distinction between diabetes and renal glycosuria. Of course, mild cases of diabetes will give results not far removed from the high limit of normality, but with renal glycosuria the sugar is rather below normal.

Acknowledgement.

Several passages in this paper are quoted almost verbatim from the works consulted. As they are in most instances modified to suit the context, I do not mark them as quotations, but here acknowledge my indebtedness to the authors.

References.

(1) A. Keogh, C. H. Melville, W. Leishman, C. E. Pollock and L. W. Harrison: "A Manual of Venereal Diseases," Second Edition, 1913, page 119.

(2) Noguchi, quoted by E. R. Stitt: "Practical Bacteriology, Blood Work and Animal Parasitology," Seventh Edition, page 271.

(3) E. R. Stitt: *Ibidem*, page 272.

(4) E. R. Stitt: *Ibidem*, page 255.

(5) G. E. Beaumont and E. C. Dodds: "Recent Advances in Medicine,"' Second Edition, 1925, page 339.

(6) David Thomson: "Gonorrhœa," 1923, page 87.

(7) G. E. Beaumont and E. C. Dodds: "Recent Advances in Medicine," Second Edition, 1925, page 87.

THE PRESENT POSITION OF OUR KNOWLEDGE AND TREATMENT OF PREECLAMPSIA AND ECLAMPSIA.[1]

By CECIL COGHLAN, M.B., Ch.M. (Sydney), F.R.C.S. (England), M.R.C.P.I., D.G.O. (Dublin), L.M. (Rotunda),
Honorary Anæsthetist, Women's Hospital, Sydney.

THE subject of this lecture is one which at the present time is exciting more interest and research than any other in obstetrics. At the outset I will stress the fact that at present we do not know the cause of this condition; I say this condition with reason, for preeclampsia and eclampsia are only different degrees of the same disease and should be covered with one name. Some authorities even go so far as to include pregnancy vomiting, habitual abortion, still-birth and *ante partum* hæmorrhage as incidents in the same disease.

Ætiology.

As we do not know the actual cause of the disease, we can only propound theories and on these theories, more or less supported by known pathological and biochemical facts, we base our treatment. No theory in itself is generally accepted, but they provide channels along which investigations are conducted.

[1] A post-graduate lecture-demonstration given at the Women's Hospital, Sydney, on January 31, 1928.

Eclampsia has been called "the disease of theories," the main ones of which are the following.

Acidosis.

The acidosis theory was suggested by Langemeister in 1903. This theory had a fair run. It was based on the fact that an increased amount of bicarbonate of soda had to be given by the mouth to produce an alkaline urine. This test for an acidosis is fallacious, as the secreting power of the kidney is impaired and the bicarbonate secreted with difficulty.

Anaphylaxis.

According to the anaphylaxis theory the fœtus and its membranes act as a foreign protein towards the maternal organism. Syncitial fragments certainly are circulating in the mother's blood stream and that an antiferment is produced is beyond question, for on its presence depends Abderhalden's test for pregnancy. But the high blood pressure, the type of the fits and the *post mortem* findings are against this theory.

Placental Toxin.

James Young[1] has recently pointed out the presence of extentive infarcts in many placentæ in eclamptics and suggests that the disease is the result of the absorption of the products of autolysis of the dead placenta. He classes as part of the same disease habitual abortion, still-births *ante partum* hæmorrhage and eclampsia, all characterized by more or less separation of the placenta. (By separation of the placenta is meant not necessarily separation from the uterine wall, but from the maternal blood stream as by thrombosis in the placental sinuses.) If the placental separation is large and incompatible with the survival of the fœtus, we get complete shutting off of the maternal circulation through the placenta and consequently no absorption of the decomposition products, but abortion or still-birth; but if it is less and compatible with the survival of the fœtus, the maternal blood circulating in the neighbouring sinuses absorbs the products of autolysis of the dead placenta with the production of eclampsia. He gives figures, too, showing an abnormal number of eclamptic cases associated with *placenta prævia*, which tend to support his theory. The weak points are that the cause of the placental separation is not explained and the products of tissue autolysis, mainly of the histamine group, tend to lower the blood pressure considerably. With regard to the first he suggests an infective organism or toxin producing a definite increase in the fibrinogen content of the maternal blood. This is normally somewhat increased in pregnancy and if clotting occurs, it would take place most easily where the stream is slowest, as it is in the maternal sinuses of the placenta. The syncitium depends for its nourishment on the maternal blood and if this is cut off, it will necrose. He has nothing to offer against the second objection.

Intestinal Autointoxication.

The intestinal autointoxication is one of the most popular theories and the one on which the Dublin treatment is founded. But beyond the undoubted benefit of the treatment and the frequent presence of indican in the urine, there is nothing to support it.

Fœtal Waste Products.

There is no evidence to support the theory of absorption of waste products from the fœtus and it is unlikely that the products of fœtal metabolism are different to those of the mother.

Depletion of Calcium Salts.

A deficiency in the calcium content of the blood leads to increased excitability of the nervous system and in the expectant mother there is certainly an increase in calcium mobility as instanced by the increased tendency to dental caries and osteomalacia; but blood calcium estimations show very little if any diminution below the normal.

Endocrine Dysfunction.

The theory of the disturbance of endocrine function has very little to recommend it beyond the fact that it is fashionable to try to explain most things in medicine that are not understood, as due to endocrine dysfunction. There are physiological changes in the endocrine system of the pregnant woman as yet not fully understood.

Bacterial Infection.

Focal infection from the teeth, tonsils *et cetera* or from the urinary tract have been suggested, but although most women harbour such foci, there is no satisfactory evidence to indicate that they play a part in the ætiology of the disease. Young has suggested the possibility of infection to cause placental separation as I mentioned in Theory III (placental toxin).

These are the theories offered to explain the ætiology of the condition, but I must say that none of them is convincing and gives us very little on which to base our treatment.

Signs and Symptoms.

Eclampsia, as we recognize it, is a disease of the latter half of pregnancy. Statistics show that it is more frequent in *primiparæ* than in *multiparæ* and hitherto it has been considered a disease that rarely recurred in a subsequent pregnancy. Young's work,[1] however, seems to indicate that recurrence is more frequent than was thought.

The first sign of impending trouble may be a slight bloating of the features and if we examine the skin of the forehead or abdomen we notice that it seems thicker than normal, the natural furrows are obliterated and it has a slight *peau d'orange* appearance. I have frequently noticed this even before detecting albumin in the urine or a rise in the blood pressure. Sooner or later we get a more or less definite generalized œdema.

The systolic blood pressure is raised in nearly every case and should be taken regularly during the antenatal period. If it rises above 140 millimetres of mercury, we should be put on our guard against the development of this disease, where it frequently rises, however, to extreme heights (280 millimetres

of mercury or more). High levels above 200 millimetres or persistence above 160 millimetres in spite of treatment are grave signs and usually indicate impending convulsions. The diastolic pressure is also raised considerably and may be as high as 120 or even 130 millimetres of mercury.

The urinary symptoms are definite. There is a diminution in the amount secreted daily and one of the earliest signs of improvement is an increase in the daily amount passed. Albumin is always present to a greater or less extent, usually greater, and when the climax in the disease is approaching may turn the urine solid on boiling.

The prodromal symptoms of the convulsive stage are: (i) Gastric disturbances, nausea and vomiting; (ii) visual disturbances, specks before the eyes, amaurosis *et cetera*, (iii) headaches; (iv) drowsiness. During the convulsive stage the fits are first tonic, then clonic and pass on to a coma, more or less severe, followed or not by recovery. During the convulsive stage we must be careful to prevent the sufferer from damaging her tongue by inserting between the teeth some article such as a piece of wood, a spoon or best of all a rubber ring pessary. The temperature rises during the fits and may reach as high as 40° C. (104° F.). With the rise in the temperature we also get a raised pulse rate.

Biochemical Findings.

The characteristic functional failure of the kidney is its inability to excrete water and chlorides and as a consequence these substances are retained in the blood and tissues, a condition of hydræmic plethora being established. The urine is greatly diminished, of normal or high specific gravity and contains a large amount of albumin. Microscopical examination reveals a large number of small hyaline or hyalo-granular casts, but rarely any epithelial casts or blood. The capacity of the kidney to excrete water can be estimated very simply. Fifteen hundred cubic centimetres of water are given by the mouth in the early morning after the bladder has been emptied and the urine secreted during the succeeding four hours is passed at half hourly intervals. Normally it is found that when the total amount is measured, it is in excess of the amount ingested and during the early part of the test there is a diuresis of about five hundred cubic centimetres in the half hour. In eclampsia, however, the total amount passed during the test is less than that ingested, the diuresis with which a normal kidney responds, is absent, the normal maximum figure of five hundred cubic centimetres in the half hour is not obtained and the amount passed in each consecutive half hour tends to remain relatively constant.

Together with the retention of water, less chlorides are excreted than are ingested. The blood chlorides, however, are only on the upper limits of normal partly owing to the hydræmia and partly owing to the retention of the chlorides in the tissues.

Examination of the capacity of the kidney for the excretion of the waste nitrogenous products of metabolism reveals little, if any, impairment and the urea concentration test gives a normal response. This test is quite simple and can easily be done by any practitioner. The non-protein nitrogen in the blood remains also within normal limits, but there is an increase in the uric acid content.

Another feature of the urine in eclampsia is the increase in the urinary diastase. The urine normally contains a starch splitting ferment and the amount present may be readily estimated by determining the quantity of urine needed to digest a known amount of starch in a given time. Usually 0·08 to 0·2 cubic centimetre of urine will digest 2 cubic centimetres of a 0·1% starch solution in thirty minutes at 37° C. By dividing the amount of starch solution used (2 cubic centimetres) by the amount of urine needed for its digestion we get the "diastatic index." Normally this varies from 10 to 30. In eclampsia the "diastatic index" is increased, but in nephritis it is very low or absent.

Other features of the blood chemistry in eclampsia are:

1. A high uric acid content.
2. An increased lactic acid content, not wholly due to muscular hyperactivity.
3. A slight hyperglycæmia.
4. A decreased carbon dioxide combining power.

At present we are not in a position to say how far this blood picture in eclampsia is due to changes in the liver and it is wise not to theorize until we have further evidence at our disposal.

Pathology.

In the examination of a woman dead of eclampsia, the examiner is struck mainly by the œdematous condition of every organ and tissue and along with this œdema there are frequently noticed small hæmorrhages into the brain, parenchymatous organs, muscles and the serous cavities; there is also a tendency to thrombus formation. Taking the individual organs, the only ones with characteristic lesions are the kidney and the liver.

The renal changes are those of an acute nephritis, with definite degeneration and necrosis of the epithelium of the convoluted tubules.

The liver in all cases is œdematous, but in most but not all fatal cases there are hæmorrhages and necrosis around the portal vessels. As these run between the lobules of the liver, we get what was once described as the characteristic periportal necrosis. Thrombotic changes also occur in the portal veins.

These, then, are the facts and fancies on which we have to base our treatment of this disease, a disease, however, which modern antenatal investigation and treatment has shown to be preventible. May I stress the fact that we should encourage every expectant mother to choose her medical attendant early after conception has occurred and that he should carefully watch her through the whole period of her pregnancy. If eclampsia should then occur in a patient for whom he is responsible, he should realize that it is a reflection on himself.

Diagnosis.

The disease should always be suspected when we discover albumin to be present during the routine examination of the urine of a pregnant woman and

this suspicion is strengthened if we have, associated with the albumin, œdema and a high blood pressure. The only other conditions from which we need to differentiate it are:

1. Pregnancy associated with a preexisting chronic nephritis—the so-called "nephritic toxæmia."
2. Pyelitis.
3. The low reserve kidney.

Having ascertained that the urine contains albumin, we should obtain a catheter specimen to confirm our finding. A microscopical examination will disclose casts, blood and pus cells. If pus cells are abundant, we may be dealing with a pyelitis which can be confirmed by ureteric catheterization. The presence of casts indicates a renal lesion, small hyaline or hyalo-granular casts occur in eclampsia, but rarely epithelial or blood casts. The simplest way to indicate the difference between eclampsia and nephritic toxæmia will be to contrast them by means of a table (see Table I).

TABLE I.

Type of Examination.	Eclampsia.	Nephritic Toxæmia.
Urine:		
Daily quantity	Small	Normal
Albumin	Large amount	Small
Urea concentration test .	Normal	Below 2%
Diastatic index	High	Low
Blood pressure ..	High and falls rapidly after delivery	Raised and the rise persists after delivery
Blood urea ..	Normal	Raised to 0·04% or more
Cardio-vascular changes	None	May be present
Eyes	Frequently no change, but œdema and hæmorrhages may occur	Albuminuric retinitis
In puerperium ..	All symptoms rapidly clear	The albumin and increased blood pressure persist for some time.

In the low reserve kidney there is a slight rise in the blood pressure and a slight amount of albumin can be detected. Everything else is normal and at the birth of the child these two symptoms rapidly clear. The outstanding characteristic is that it recurs with every pregnancy and in the subsequent pregnancies the condition is not aggravated.

Treatment.

Having determined the presence of eclampsia, our next problem is the treatment of the condition. In the early stages of the disease all authorities are agreed as to the efficacy of rest and promotion of elimination. The patient is sent to bed and her diet restricted, but there is no need to deprive her entirely of meat foods as the blood urea is normal and the kidneys can concentrate well. If she is constipated, an enema is given at the start of the treatment. Large doses of a saline cathartic are given three times a day and continued for several days; at the Rotunda Hospital we used to give ninety cubic centimetres (three fluid ounces) of *mistura sennæ composita* to which an extra four grammes (one drachm) of magnesium sulphate were added for each thirty cubic centimetres (one ounce) of the mixture. Plenty of fluid is administered to flush the kidneys and to make up for the loss due to the purgation. *Potus imperalis*, lemon drinks, weak tea, milk and water or just pure water must be given; about four and a half litres (eight pints) are given in the twenty-four hours. If the albumin and œdema are considerable, stop all food and milk is included as food for a couple of days or until the urine has increased in amount to about a litre (forty ounces) a day. After several days of treatment a definite improvement is usually noticed and the food allowance may be increased and the purgation lessened, but a regular watch must be kept on the patient for the rest of the pregnancy, the purgative being increased and the diet restricted if occasion demands it, which happily is very rarely.

If she does not respond to this treatment or if, when we first see her, she is suffering from the prodromal symptoms of the convulsions (gastric and visual disturbances, headache, restlessness *et cetera*) or she is actually in convulsions or coma, we must start the more active treatment immediately. Owing to the uncertain ætiology of the disease, the treatment of the more severe symptoms of the disease is extremely varied. There are two opposing schools, the one advocating a rapid termination of the pregnancy, the other advising no interference at all with the course of the pregnancy, but treatment to eliminate the supposed toxins and to control the convulsions. The former school terminates the pregnancy by induction of labour, Cæsarean section or *accouchement forcé*. The other school, known as the conservative school, promotes elimination and controls the convulsions by means of copious enemata and colonic lavage, hot packs, infusions with saline solution or bicarbonate of soda solution and drugs such as morphine, chloral, bromide *et cetera*.

It is now almost generally admitted that any operative interference with the course of the pregnancy, such as *accouchement forcé* or Cæsarean section amounts almost to signing the patient's death certificate. Let me give the figures from a report on over 2,000 cases collected from various hospitals over a period of ten years and presented to the Congress of Gynæcology and Obstetrics in England in 1922 (see Table II).

TABLE II.

Method of Treatment.	Percentage Mortality.	
	Mild Cases.	Severe Cases.[1]
Natural delivery	4·5	36·9
Assisted delivery	5·6	31·7
Induction	6·6	26·4
Cæsarean section	11·3	46·3
Accouchement forcé	18·1	63·1

[1] Severe cases are those which exhibit any two of the following symptoms, namely, pulse rate over 120, temperature over 39·4° C. (103° F.), more than ten fits, suppression of urine, deep coma, sufficient albumin to turn urine solid on boiling (Eden).

Cæsarean section has been extensively used in America and Germany, but even these countries are now turning more towards the expectant methods. Induction gives comparatively good figures owing to the fact that it is mostly used after the patient has improved under conservative treatment. The usual explanation of the bad result of active treatment is that it is the effect of the added shock to an already hypersensitive nervous system, but Dr. Stander,[4] of Montreal, suggests that it is due to the prolonged anæsthesia necessary for the operation and he is at present trying on a series of cases the effect of Cæsarean section performed under spinal anæsthesia.

The two types of expectant treatment mostly used are those known respectively as "the Dublin method" and "Professor Stroganoff's method." Some schools modify one or other of these methods, but as the original form of treatment in either case gives better results than any published modifications, I would strongly advise that they should not be tampered with. The mortality figures for the Rotunda Hospital were 8·8% in 214 cases over a period of twenty years, while Professor Stroganoff reports a mortality of only 1·7% in cases treated under his personal supervision. Others have not been able to reproduce the wonderful figures of Professor Stroganoff and hospitals where his technique has been carefully followed, report mortality rates averaging between 9% and 10%. As the two treatments are based on such different principles I will give a detailed description of them both.

When the patient shows signs of impending fits she should, if possible, be removed to a hospital where the treatment can more accurately and rigidly be carried out. The transport of a patient who is in or threatening convulsions needs the greatest care. Someone skilled in the treatment of the disease should accompany her and she should be deeply under the action of morphine. Two cases have recently come to my notice in which the patient arrived dead at hospital and one of them almost certainly died from asphyxia during the journey.

The Dublin (Rotunda Hospital) Method of Treatment.

The patient is placed in a room by herself and the room is kept darkened and warm. She is placed in the Sims's (left lateral) position with the buttocks at the side of the bed and the head so arranged with pillows that the mouth is dependant and thus permit the secretions to readily drain out. The stomach is washed out with warm bicarbonate of soda solution, four grammes to 600 cubic centimetres (one drachm to the pint). When the return is free from any sign of gastric contents, syphon the fluid from the stomach as completely as possible, then run in one hundred and twenty cubic centimetres (four fluid ounces) of the strong *mistura sennæ composita,* followed by 600 cubic centimetres (a pint) of the bicarbonate of soda solution and withdraw the tube. Following the gastric lavage or concurrent with it if two physicians are available, the colon lavage is performed. For this several gallons of a soap and water solution are used, followed by about nine litres (two gallons) of the bicarbonate of soda solution. A number 24 stomach tube is used; this is passed into the rectum which is washed out with a couple of pints of the soap solution. The finger is inserted alongside the tube and is pushed in until the upper fold of the rectum is felt and the tube guided past this. This is sometimes a rather difficult procedure, but it is helped by allowing the fluid to pass through the tube. Once the tube is guided past this obstruction it can readily be pushed in for about another eighteen inches. If the tube is properly passed two to three pints of fluid can be syphoned in and out quite easily, but if the tube is only in the rectum only up to about one and a half pints can be passed when the solution returns alongside the tube. For the lavage up to eight gallons of fluid are used. It returns at first contaminated with fæcal matter, then clear, then more fæcal matter and then clear once more when the fluid is changed from the soap solution to the bicarbonate of soda solution and between one and two gallons of this run in and out. Finally about 850 cubic centimetres (one and a half pints) of this solution and 120 cubic centimetres (four ounces) of the *mistura sennæ composita* are run in and the tube withdrawn. If a fit occurs during the treatment, "carry on." At the conclusion of the colonic lavage empty the bladder and keep a careful record of the quantity of urine secreted subsequently.

This treatment is repeated in eight hours and again a third or even a fourth time if the patient is comatose, but rarely are more than two necessary. The second colonic lavage often produces a most astonishing fæcal result, for by now the saline purge that had been given at the previous treatment, has emptied the upper part of the intestinal tract.

Following this lavage the bowels usually act spontaneously and frequently.

At the conclusion of each treatment the patient is placed in a warm bed (it is an advantage to have two in the room) after being thoroughly dried. A large linseed poultice is applied to the back covering it from the scapula to the sacrum. The Sims's position is maintained, but is occasionally changed from left to right and *vice versa.* Care should be taken to prevent the bowel discharge, which may be continuous, from fouling the patient. Improvement is noticed in the great increase in the flow of urine, which may reach to between three to six litres (one hundred and two hundred ounces) in the twenty-four hours. Only in cases that do not respond to the second lavage is a submammary infusion of bicarbonate of soda solution given.

When I was at the Rotunda Hospital morphine was not used, although it had been previous to the mastership of Dr. FitzGibbon. During the last few years their figures have been even better than I have quoted and in 1925 there were no deaths in sixteen cases.

With the patient recovered from the coma, the fits discontinued and the urine being passed freely, the question now arises: "What shall be done with

the pregnancy?" At the Rotunda Hospital we left the case alone if everything seemed to be going well, but if there was any sign of a relapse, such as increasing albumin in the urine, a decrease in the amount of urine passed or a rise in the blood pressure, we placed the patient on the early treatment and on improvement induced labour.

Some of the English schools, for example, Queen Charlotte's, use "Veretrone" to control the blood pressure, do not use stomach lavage and induce labour on the third day after the last fit.

Professor Stroganoff's Treatment.

Professor Stroganoff's method has as its cardinal principle that the fits must be controlled. The patient must be removed from all sources of external irritation and so is placed in a quiet, darkened room and all manipulations and injections are carried out under light chloroform anæsthesia. A hypodermic injection of 0·015 gramme (a quarter of a grain) of morphine is given immediately, followed in one hour by two grammes (thirty grains) of chloral hydrate, in three hours by 0·01 gramme (one-sixth of a grain) of morphine, in seven hours by two grammes of chloral hydrate, in thirteen hours by the same quantity of chloral hydrate and in twenty-one hours again by the same quantity of chloral hydrate.

The chloral hydrate is given by the rectum if the patient cannot swallow. If at the end of twenty-four hours the patient is still undelivered, one to 1·3 grammes (fifteen to twenty grains) of chloral hydrate are given three times a day. If the fits recur in spite of the treatment, venesection to the extent of four hundred cubic centimetres is performed. During the treatment the patient is encouraged to consume, if conscious, quantities of fluids such as weak tea, milk and water *et cetera* and she is kept warm with hot bottles. When fits occur, they are controlled by chloroform anæsthesia.

This treatment may be modified to suit the condition. That outlined above is sufficient for the mild to moderate case, in the more severe the amounts of the drugs can be increased and further doses given. The course of the pregnancy is not interfered with at all.

To a country practitioner with the patient away from hospital, this method has decided advantages over the Dublin method.

A method of treatment recently tried is the intravenous or intramuscular injection of a solution of magnesium sulphate, a known nerve depressant; intravenously twenty cubic centimetres of a 20% solution or intramuscularly ten or more cubic centimetres of a 25% solution are used. A series of 142 patients treated by the intravenous method are reported from the Los Angeles General Hospital with a 9% mortality.[2] In this series from one to twenty injections were used.

Stander, of Montreal, however, experimenting on dogs shows that magnesium sulphate produces fatty changes in the liver and lowers the carbon dioxide combining power of the blood, which makes it appear that magnesium sulphate may do harm.[3] He also shows in another paper[4] that the administration of all anæsthetics produces a reduction of the carbon dioxide combining power of the blood and fatty changes in the liver and the kidneys; these latter are not typical of eclampsia, but when dealing with a disease in which it is known that there is liver and kidney damage, I am loath to recommend anything that affects these organs further. Chloroform reduces the carbon dioxide combining power of the blood less than ether or nitrous oxide, probably on account of the need to produce partial asphyxia in the administration of the latter two anæsthetics. Morphine and chloretone give rise to no lesions, but chloral produced an intense congestion.

He is at present working on a modified Stroganoff technique, not using chloroform and venesection and reports a mortality of 2% in mild cases, but he suggests an urgent need for better treatment of the more severe cases.

As endocrine therapy has been the fashion it is only natural that thyreoid extract has been used in the treatment of this disease, with reported success in a few cases, but as it was not used alone the report is of little value.

Complications.

Respiratory distress and cyanosis are the result of pulmonary œdema and are best relieved by oxygen administration, but see that the respiratory passages are clear and not obstructed by mucus *et cetera*. On recovery the greatest danger is the onset of pneumonia and during the whole treatment this should be carefully guarded against.

Cardiac distress is indicated by a rising pulse rate associated with a falling blood pressure and should be checked by the administration of digitalin. If a sudden collapse should occur camphor and pituitrin are useful and oxygen should be administered.

Suppression of urine is a very bad sign. There is nothing that can be specially done to relieve it.

If labour should come on, allow it to proceed, but help it with forceps in the second stage if there should be any delay. As a rule labour is rapid, as there is no resistance by the patient to the depression of the perineum.

Prognosis.

A neglected case of eclampsia is always serious. If the condition is detected early and treatment is instituted, we may claim that practically all patients recover. In the more severe cases it is difficult to prophesy what will be the course of the disease; some patients die with one fit, others recover after many fits; but usually the greater the number and the more frequent the fits, the worse the outlook. The persistence of a high blood pressure, the onset of jaundice and anuria with no reaction to the hot pack are very ominious symptoms. The death of the fœtus usually reacts favourably on the disease. Usually while the pulse remains good, the outlook is good and the presence

of definite œdema is if anything a favourable symptom. After delivery all symptoms clear up with remarkable rapidity and it is unusual for the patient to get a recurrence during a future pregnancy, although the work of Young,[1] quoted above, tends to show that this is not so certain as was previously thought.

Conclusions.

1. Eclampsia is a disease of pregnancy which if detected early has a very favourable prognosis.
2. With more efficient and universal antenatal treatment the convulsive form of this disease should be rare.
3. The occurrence of eclampsia with convulsions in a patient who has been under care for some time, is a reflection on the attendant.
4. The ætiology and pathology of the disease are still uncertain.
5. The best results are obtained by the use of conservative measures in the treatment of the disease.
6. Operative measures to terminate the pregnancy should be strongly condemned.
7. Anæsthetics are detrimental, especially those that produce an anoxæmia.

References.

(1) James Young: "Recurrent Pregnancy Toxæmia," *British Journal of Obstetrics and Gynæcology*, Volume XXXIV, Number 2, Summer Number, 1927, page 279.

(2) E. M. Lazard, John Irwin and John Vruwink: "Intravenous Magnesium Sulphate Treatment in Eclampsia," *American Journal of Obstetrics and Gynecology*, Volume XII, Number 1, July, 1926, page 104.

(3) H. J. Stander: "Clinical and Experimental Studies on the Toxæmias of Pregnancy," *American Journal of Obstetrics and Gynecology*, Volume XIII, Number 5, May, 1927, page 551.

(4) H. J. Stander: "Studies in Anæsthesia, Anoxæmia, Anhydræmia and Eclampsia," *American Journal of Obstetrics and Gynecology*, Volume XII, Number 5, November, 1926, page 633.

VASCULAR DISTURBANCES AS AN EXPLANATION OF NERVOUS SYMPTOMS.[1]

By ARTHUR E. MILLS, M.B. (Sydney),
Professor of Medicine, The University of Sydney; Honorary Physician, Royal Prince Alfred Hospital, Sydney.

EVER since I read that very suggestive little book by the late Sir James Mackenzie entitled "The Interpretation of Symptoms," I have been endeavouring to get an understanding of the meaning of the various symptoms that patients complain of, how they arise, on what anatomical, physiological or pathological bases they depend.

The attempt has not been altogether in vain. It has enabled me to listen with more equanimity to the recital, oft-times very tedious, of the patient's symptoms. And when each symptom, however vague, becomes a subject for interpretation or a problem for solution one's interest is greatly aroused. It may not be possible to interpret the problem fully, but at least an attempt may be made. The endeavour is worth while.

Many years ago I was impressed with the fact that pain was a prominent feature in many vascular disturbances. In thrombosis of the veins of the leg which, as you know, is common enough in the puerperium, the first symptom is pain, sudden and severe. At first there is nothing to show what has caused the pain, but after the lapse of some hours the white, swollen leg tells us that venous thrombosis has occurred, but why the pain? And this was the only symptom complained of.

In cases of *endarteritis obliterans* or what we might term *thrombo-angeitis obliterans*, a term that is more embracing, pain is oft-times very pronounced and has certain characteristic features.

A friend of mine suffered from such a vascular disturbance of his foot. The pulse in the anterior and posterior tibials was absent, or almost so. The pain in the foot became unbearable, especially in the cold weather. He could not bear his foot hanging down. He became incapacitated and his sufferings led him to resort to morphine in increasing doses. Eventually in order to relieve his pain his foot was amputated. The vessels were narrowed and blocked to such an extent that practically no bleeding resulted when the tourniquet applied to prevent bleeding was removed.

But what was the cause of the pain?

A hotel keeper suffered from such pain in his legs after walking some distance that he could not continue. He was forced to rest for a time. With rest the pain disappeared, only to reappear in a little time after walking was resumed. As the days went by, he noticed that the pain came on after shorter and shorter periods of walking, so that he found he could not walk more than fifty yards without pain. Finally after standing for any length of time the pain in his legs became so severe he was forced to sit to get relief.

This is a case of intermittent claudication; but again the question arises: Why the pain?

The real cause for the pain in these and similar cases where pain and deficient blood supply are associated, was made clear to me when I was asked to see a colleague who suffered from a pain in his foot.

The history was that while walking a short distance to catch the ferry boat he felt a sudden pain in his first and second toes. When he reached the wharf the pain had increased to such an intensity that only with the greatest difficulty could he walk back home. He was compelled to go to bed, where he remained for some weeks. He could scarcely bear his toes to be touched, nor could he allow the foot to hang down because in this position the pain was intolerable. Some days later an area on the side of the heel of the same foot became suddenly painful and tender. The pain was even more intense than in the toes. The skin of this painful area in a day or two showed signs of commencing gangrene. Eventually it sloughed away and left a very painful ulcer. There can be no doubt that the pain and tenderness and gangrene of the skin of the heel were the result of a complete occlusion of the blood supply to it; and there can be no doubt that the pain and tenderness of the toes were due to a partial, but almost complete, obliteration of the vessels supplying the skin of the toes.

[1] Read at a meeting of the Sections of Neurology and Psychiatry and of Medicine of the New South Wales Branch of the British Medical Association on December 1, 1927.

When ethyl chloride is sprayed on the skin, the first sensation is one of cold from stimulation of the nerve endings. This sensation of cold becomes more and more intense and is succeeded by a sudden and acute pain just before or at the time the skin becomes blanched and frozen. Immediately afterwards all sensation vanishes, the part is momentarily dead and the passage and conduction of all nerve impulses are blocked.

I would have you note that cold as a stimulus may blanch the skin without giving rise to pain. Witness the white, dead fingers of patients whose capillary circulation responds so readily to the influence of cold. Such patients complain only of cold and numbness, not of pain, but that I think is due to the fact that with cold as the stimulus the threshold for pain is high and only when the stimulus is very great is the threshold overstepped.

But another question arises: "Is the pain that results from the application of great cold, due directly to the cold on the nerve endings or is it caused indirectly by the cold acting on the blood vessels producing capillary constriction leading to anoxæmia of the nerve endings in the skin?" That capillary blockage does cause great pain is evident from the case already quoted and as the result of cold sufficiently great to cause freezing of the skin.

In cases of venous and local arterial thrombosis and *thrombo-angeitis obliterans* and in cases of intermittent claudication the nerve endings in the skin or the muscles become hypersensitive to an extreme degree so that the slightest irritation, even the lightest touch, applied to the skin or slight pressure to the muscles causes great pain. In these cases there is one condition common to them all—diminished blood supply and that means oxygen want—and it is to this condition that the hypersensitiveness is due.

I feel sure that not enough attention is paid by clinicians to nerve endings and nerve cells. It is the nerve endings that receive and respond to their appropriate stimuli, be it ever so slight, for they are structurally and physiologically adapted so to do. The nerve fibres conduct nerve impulses received from the nerve endings to the nerve cells and these in their turn respond to the slightest stimulus so received. The threshold of response of nerve endings and nerve cells to appropriate stimuli is very much lower than that of nerve fibres and this threshold may be still further lowered by a diminished vascular supply leading to varying conditions of oxygen want.

Nerve cells, both sensory and motor, when rendered hypersensitive, respond to ordinary stimuli in the same exaggerated way as normal cells respond to excessive stimuli.

A condition of oxygen want may be brought about from local causes, for example thrombosis, embolism or hæmorrhage or *thrombo-angeitis obliterans* or from congestion or œdema or from vasomotor changes or from general causes such as carbon monoxide poisoning, mountain sickness and profuse hæmorrhage. In the last condition painful cramps of the muscles may be experienced.

All these various causes have at any rate one common end result—interference with the blood supply which results in a want of oxygen to the tissues—and that end result is the real cause of the symptoms, as may be seen from a consideration of the following pathological conditions: A vascular lesion of the *thalamus* gives rise to Roussy's so-called thalamic syndrome, of which pain, persistent, paroxysmal and intolerable and over-response to peripheral stimuli are the most characteristic. How does this pain arise?

How remarkably like the pain found in a case of vascular obstruction of the skin, in which, as we have seen, the only satisfactory cause for the pain was deprivation of the nerve endings of their blood supply, that is, anoxæmia. Now a vascular lesion leading to anoxæmia of the nerve cells of the *thalamus* may in a similar way bring about a hypersensitivity of the cells, so that they respond in a most exaggerated manner to stimuli that ordinarily would only cause slight discomfort, for example, gentle traction on the hairs of the eyebrows or scalp of the affected side evokes great pain, drawing the head of a pin over the surface of the skin of the affected side is unbearable.

Associated with this state of irritability or hyperfunction of nerve cells there are other signs which point to loss of function, such as interruption of conduction of both motor and sensory impulses. Seeing that both hyperfunction and loss of function arise from the same vascular lesion, it can only mean that certain nerve structures are quite put out of action, while others are rendered more irritable. The nerve cells of the *thalamus,* the cell stations in the sensory pathway to the sensory cortex, now rendered highly hypersensitive by defective blood supply, that is, by oxygen want, give rise to pain and this pain is referred to those peripheral nerve endings which are associated with them. When these nerve endings are subjected to a mild painful stimulus the effect is as if a severe painful stimulus was applied.

I have long pondered over the causation of this condition and from a consideration and fuller knowledge of the effects of vascular disturbances in nerve endings and nerve cells there appears little doubt that vascular lesions, bringing about a condition of oxygen want, offer a satisfactory explanation.

In conditions of inflammation of posterior spinal root ganglia—in so-called *herpes zoster*—the painful symptoms bear much resemblance to those met with in thalamic disease. Now an inflammatory affection is characterized by great vascular disturbance, leading to the outpouring of plasma and migration of blood cells. The circulation at first increased, later becomes impeded and the tissues in the inflamed area suffer from want of oxygen. We are too apt in such conditions, I think, to ascribe the pain to pressure and tension on nerve structures. If pressure or tension were the cause, why should the pain persist, as it so often does, for weeks and months, long after the conditions giving rise to pressure or

tension have passed away? But after the acute process has ended, when the blood fluids and cells and tissue cells have all been absorbed, when now there remains nothing to cause tension, there may still remain vessels so damaged and thrombosed that the nerve cells are starved of oxygen and just that degree of oxygen want is brought about which causes hypersensitiveness and leads to excessive response to mild stimuli.

The symptoms that are to be seen in this common affection, vary greatly. The pain is often felt many days before the vesicles appear. In some cases the vesicles are few, but the pain is intense and it persists for a long period. In other cases, while the vesicles are numerous, the pain is not very pronounced and may soon disappear. Assuming, as I think we are entitled to do, that the vesicles indicate great hyperactivity of the trophic nerve cells, as the pain indicates heightened activity of the cells subserving the conduction of pain impulses, then oxygen want of varying grades resulting from vascular disturbances will explain the varying symptoms. As a result of great oxygen want many of the nerve cells will die, even as they do in cases of poliomyelitis. The cells, responsible when damaged for vesicle formation, may suffer more than those which conduct pain impulses or *vice versa*. Of the two kinds of cells we are considering, more cells of one function may be affected than the cells of the other function.

Now, as we have seen, ordinary stimuli applied to highly sensitive nerve endings will evoke the sensation of pain, so also the same effect will be brought about if ordinary nerve impulses from normal nerve endings reach nerve cells in a highly sensitive state. In both conditions the threshold to stimuli is much lowered.

The same physiological law holds good both for sensory and motor nerve cells. There is abundant evidence in support of such a statement. The cells of the respiratory centre give the best evidence of the effect of oxygen want on motor cells. It has often been pointed out that those cells which are the oldest from the evolutionary standpoint are the most stable and the best able to withstand destructive influences. The respiratory cells belong to the oldest class, they maintain their functional activity long after most of the other cells of the brain have ceased to work. Patients rendered unconscious as the result of an accident or from cerebral hæmorrhage or from advanced degrees of oxygen want, may remain unconscious and show no signs of life other than that they breathe and that their hearts beat up to the moment of death. Despite their stability and resistance, the cells of the respiratory centre show extraordinary susceptibility to both oxygen want and increase of hydrogen ions in the blood.

The nerve cells of the respiratory centre in an environment of oxygen want either from carbon monoxide poisoning or from mountain sickness—the result of breathing air at low barometric pressure—or from anæmia of the brain from hæmorrhage or cardiac failure, become extremely sensitive. Their threshold for stimulation is now greatly lowered, so that they respond to normal or even subliminal stimuli in an exaggerated manner. The nerve impulses sent out to the respiratory muscles are much larger and inspiration and expiration are much deeper than normal. Indeed, we may accept it as a fact that deeper respirations always mean exaggerated discharges from the respiratory centre, but such increased discharges may result, as has already been pointed out, from (i) a hypersensitivity of the cells of the respiratory centre or from (ii) excessive stimuli acting upon the centre, such as an increased hydrogen ion content of the blood or through the vagus when its nerve endings are rendered hypersensitive by oxygen want, as occurs in cases of pulmonary embolism and pulmonary œdema.

Perhaps the most striking effect of the action of oxygen want on the respiratory centre is periodic breathing of which Cheyne-Stokes breathing is the most common pathological variety.

Quite recently I saw an example of periodic breathing in a little child who had tuberculous meningitis. The child was unconscious, the fontanelle bulged to a considerable degree despite the fact that the child had for days previously vomited all the food she had taken, so that the bulging must have been due to an excess of cerebro-spinal fluid which, as will be seen later, must displace the blood within the veins and venous sinuses and lead to anoxæmia of the brain. So the respiratory centre would be in an environment of oxygen want. In this case there were a series of five respirations followed by a period of apnœa and this type of breathing continued for hours.

A similar type of periodic breathing may be produced in normal people, as Haldane has pointed out, by simple forced breathing for a period of about two minutes.

Pembrey and Allen showed that the well-known pathological form of periodic breathing, known as Cheyne-Stokes breathing, is abolished by giving the patient pure oxygen to breathe. This observation indicates with great certainty that ordinary pathological Cheyne-Stokes breathing is caused by want of oxygen participating in the excitation of the centre.

The general view regarding the dyspnœa of pulmonary embolism, of which I have had personal experience, is that it is due to the putting out of functional activity of a certain amount of lung tissue. Such a view, I think, cannot be maintained except when a very large branch of the pulmonary artery is blocked.

But in most cases where only a comparatively small arterial branch is plugged, the dyspnœa may be very pronounced. The blockage leads to an infarct, but around the infarct there will necessarily be an area of œdema. The vagal nerve endings within the infarct at first will be violently shocked and become very hypersensitive as a result of oxygen want. Their hypersensitivity, however, will soon disappear because owing to complete deprivation of oxygen, these nerve endings will then cease to function. Meanwhile, however, great impulses will travel from them and from those in the œdematous

zone to the respiratory centre, which in turn will respond by sending violent discharges to the respiratory muscles, causing intense dyspnœa. In such cases too the dyspnœa is of short duration and this will correspond to that short period between the onset of the embolism and the death of the nerve endings.

Again, in oxygen want as a result of mountain sickness or in a local vascular disturbance, affecting the vestibular nuclei, caused by thrombosis of the posterior inferior cerebellar artery, one of the main symptoms is intense vertigo. Vertigo, as I have shown elsewhere, is in most cases the expression of hypersensitivity of the vestibular nerve endings or nerve cells. The discharges from these nerve endings or nerve cells so sensitized may be so great that equilibrium is lost and overaction of muscles in an effort to maintain a normal equilibrium may result in the patient falling or being thrown to the ground.

Vomiting may be cited as a further example of the physiological effect of oxygen want. Vomiting is a reflex act involving the coordinated action of many muscle groups. This act may result from the effects of general oxygen want on the cells of the vomiting centre, as occurs in mountain sickness, or anæmia of the brain from cerebral hæmorrhage or from œdema of the brain. This reflex act may result from normal stimuli acting on a very irritable vomiting centre or from excessive afferent stimuli acting upon a normal centre.

The centre may be hypersensitive as a result of general oxygen want, as occurs in mountain sickness or from anæmia of the brain, the result of rapid great loss of blood, or from hæmorrhage into the brain, or from toxæmia of infectious diseases such as influenza, pneumonia or scarlatina.

There is much to be said for the view that the toxæmia of infectious disease may not act directly as a stimulus to the vomiting centre, but indirectly by bringing about anæmia of the centre. It is well known that in the early stages of an infectious disease the patient feels cold. He may have a rigor. Now we feel cold when our skin is cold, despite the fact that our internal temperature may be very high and our skin feels cold when little blood circulates through it. Evidently then the infection has a very profound and widespread effect on the general circulation to cause a general depletion of the blood supply to the skin. This widespread effect can be brought about only through the influence of the vasomotor centre. If the toxæmia of the infection can bring about through the agency of the vasomotor centre a greatly diminished blood supply to the skin, may it not in like manner affect the blood supply to the brain and produce anæmia of the vomiting centre?

I suggest, too, that those psychical influences aroused by such stimuli as a gruesome sight, an obnoxious odour, a vile taste or violent pain, acting through the nerves of sight, smell, taste and those subserving pain, may produce vomiting by their effect on the vasomotor centre, leading to anæmia of the brain and a condition of oxygen want around the vomiting centre. The question is worthy of much consideration, for vomiting is a very common symptom and often of great diagnostic significance.

It is well known that nerve tissues, that is, nerve cells and their processes, with their specially adapted nerve endings, cease to function and soon die when their oxygen supply is cut off. It is true nerve cells may recover if the supply of oxygen is not withheld for too long a period. Haldane has pointed out:

> If pure anoxæmia is produced suddenly as by breathing pure nitrogen, hydrogen, methane, or nitrous oxide, loss of consciousness occurs quite suddenly and with no previous warning symptoms. Thus, too, a miner who puts his head into a cavity in the roof full of pure, or nearly pure, methane, drops suddenly as if he had been felled.

But if the state of oxygen want is a gradually progressive one, then we may see those diverse symptoms which express varying degrees of anoxæmia, as they affect different nerve cells.

After an explosion in a coal mine carbon monoxide is produced in large quantities and constitutes a considerable percentage of the air in the mine. Now, carbon monoxide is an inert and non-poisonous gas. It has a greater affinity for hæmoglobin than oxygen, so that once it combines with hæmoglobin it is not easily displaced. When air containing a high proportion of carbon monoxide is breathed, much carboxyhæmoglobin is formed. The hæmoglobin as an oxygen carrier—and this is its especial function—is rendered useless and the nerve tissues, the most susceptible of all tissues, soon suffer from oxygen want.

In carbon monoxide poisoning cyanosis is absent. Cyanosis is the result of excess of reduced hæmoglobin in the blood. Instead of an excess of reduced hæmoglobin there is an excess of carboxyhæmoglobin in the blood. This compound of hæmoglobin has a characteristic scarlet colour and gives a scarlet or pink colour to the skin of the patient. On the other hand in a faint or syncopal attack the patient is at first pale from diminished blood supply to the skin, later the patient becomes cyanosed. With the onset of cyanosis—and this implies absence or diminution of oxyhæmoglobin—there is a state of oxygen want. We may witness the very same symptoms in this state that we may see in the corresponding phase of an epileptic fit. The muscles of the body become rigid, then show convulsive movements. There are violent efforts on the part of the respiratory centre which at last overcome the spasmodic closure of the glottis. Then when respiration is reestablished, the cyanosis disappears and with it the convulsive movements. But observe, the rigidity of the muscles and their convulsive movements occurred during the stage of oxygen want.

In certain stages of progressive carbon monoxide poisoning there are the same symptoms, unconsciousness, rigidity and convulsions, as are to be found in a syncopal attack. There does not appear to be any other cause for the symptoms mentioned than oxygen want acting on the motor cells of the

cortex rendering them more irritable and causing those excessive discharges from them which bring about the muscular rigidity and convulsions.

When rarified air, that is, air at a low barometric pressure, such as is found at altitudes of fifteen to twenty thousand feet, is breathed, the effects are very various and widespread. The following are some of the symptoms observed by the members of the Anglo-American Expedition to Pike's Peak in 1911: Headache, nausea, vomiting, abdominal discomfort, diarrhœa, breathlessness on slight exertion, Cheyne-Stokes breathing and marked cyanosis. I would like to discuss all these symptoms with you and to show that they are dependent upon oxygen want, but time will not allow me. I propose therefore to devote the rest of the time at my disposal to a discussion of that most common symptom—headache.

But before doing so I would like to read a short extract from the report of the before-mentioned expedition.

> Among the numerous visitors who came up by train and stayed only about three-quarters of an hour, the most marked and almost universal symptom was blueness of the lips, cheeks *et cetera*, accompanied by great hyperpnœa on exertion. As a rule there was no marked discomfort, but some fainting was observed occasionally, as well as vomiting. One press representative who came to "interview" us became so alarmingly blue and faint that we gave him oxygen which revived him at once and immediately restored his colour and spirits. He continued all right for a few minutes and then again became blue and faint and was again completely revived by oxygen, after which he hurried into a descending train. In the case of two friends who stayed several hours severe headache developed on the way down and continued till night.
>
> Among those who walked up or came on donkeys, the symptoms were much more general and severe. The blueness was more marked and nausea, vomiting, headache and fainting were extremely common. Many persons walked or rode up during the night to see the sunrise, especially on Sunday morning and the scene in the restaurant and on the platform outside can only be likened to that on the deck or in the cabin of a cross-channel steamer during rough weather. The walkers straggled in one by one, looking blue, cold, exhausted and miserable, often hurrying out again to vomit. Some lay on the floor, blue and faint. Others were able to swallow some coffee, but very few had the heart to look at the magnificent sunrise.
>
> One alarming case of a woman who became unconscious during the ascent occurred during our stay, but she was brought down in a special train and recovered under medical care. We saw several alarming cases of persistent fainting, but all recovered after a time. Bleeding from the nose *et cetera* has sometimes been described as a symptom of mountain sickness, but we did not observe any case of bleeding.
>
> All the untoward symptoms seemed to be due directly to the effects of oxygen want upon the tissues, and in particular upon the central nervous system. This was proved by the immediate and striking relief obtained through inhalation of oxygen. The respiratory symptoms may readily be interpreted from what has been said of the regulation of respiration. The hyperpnœa so easily produced by muscular exercise at these altitudes is due to the increased oxygen consumption accentuating the existing oxygen want. This together with the increased production of carbon dioxide affects the respiratory centre.

Headache.

Resuming our discussion let us now consider headache. I would stress the fact that pure oxygen want, as is found in mountain sickness and in mild cases of carbon monoxide poisoning and profound anæmia causes headache. The question before us is how is it produced, not only in these cases, but in many disorders in which it is a more or less pronounced symptom?

Now, by headache I mean the pains and aches of various kinds which arise and are felt within the skull, not those pains or aches of the head which arise here, as in other parts of the body, from affections of the tendons or fibrous structures attached to the outside of the skull and known as fibrositis.

Let us bear in mind that within the skull we have the brain with its membranes, the arteries and veins with their perivascular spaces, the venous sinuses, the cerebro-spinal fluid and certain sensory nerves distributed to the membranes, chiefly from the trigeminal and spinal nerves.

Now the brain, though it is the organ through which we appreciate pain, may itself be assaulted in various ways without evoking a sensation of pain —blood may be extravasated into it, its blood supply may be grossly interfered with, it may be distorted and pressed upon, parts of it may be destroyed by the growth of tumours, it may be subjected to great pressure, as is found in great increase of intracranial pressure, various parts of it may be removed by the knife or cautery, but in all these cases headache may not be felt. And the reason is that the assaults mentioned are not the appropriate stimuli for the production of headache.

It is, of course, well known that adequate stimuli, applied to certain nerve endings or fibres or nerve cells, are translated into nerve impulses which, being transferred to the brain, evoke in our consciousness the sensation of pain and are referred to the site of stimulation, but they do not cause headache. *Tic douloureux* is an affection of the Gasserian ganglion, but the most severe cases of this disorder do not cause headache, but pain referred to the peripheral distribution of the various branches of the trigeminal nerve; just as posterior root ganglionitis causes pain referred to the peripheral distribution of those spinal nerves connected with the affected cells.

Similarly, when the cells of the *thalamus* or sensory cortex become hypersensitive and receive normal appropriate impulses, the result of stimuli applied to peripheral nerve endings in various parts of the body, great pain is experienced and is referred to the site of stimulation, but headache does not result.

It follows then that stimuli applied to hypersensitive nerve endings situate within the skull, in the bones or membranes, lead to nerve impulses which, being conducted to the *thalamus* and sensory cortex, are there interpreted as pain and as pain referred to the site of stimulation, that is pain in or within the skull and pain in or within the skull is headache. Looked at in this way headache is produced in the same way as pain is produced, say from a whitlow or from an inflamed appendix.

Similarly when nerve impulses, the result of appropriate stimuli to normal nerve endings within the skull, that is in the membranes and bones, reach certain cells of the *thalamus* and sensory

cortex in a hypersensitive state, the effect will be pain within the skull and the pain will be referred to the site of stimulation.

It is clear, therefore, that in both conditions described the site of the headache will correspond to the position of the nerve endings which are stimulated. If such nerve endings be situated in the frontal, parietal or occipital regions, the headache will be interpreted as being in those regions.

Now it is well known that the membranes, when the seat of inflammation or gummatous infiltration or tumour formation, cause great pain and in cases of tumour or inflammation of the bone pain is experienced. In meningitis there is the characteristic engorgement of the vessels together with the accompanying œdema. Such engorgement and œdema by simple pressure on nerve endings in the inflamed areas may evoke nerve impulses which will be interpreted as headache. On the other hand the congestion and œdema may exert sufficient pressure on the vessels in the inflamed area, so that the circulation of the affected part becomes defective and leads to oxygen want. The nerve endings then in an environment of oxygen want will become hypersensitive and headache will result, as has already been shown.

After the removal of a considerable quantity of cerebro-spinal fluid by lumbar puncture headache is very common and oftentimes very severe. How is such a headache produced? We must bear in mind that the skull is an unyielding box and the brain tissue itself is incompressible. The amount of blood within the arteries and veins and nervous sinuses may vary and so may the amount of cerebro-spinal fluid. If there be much cerebro-spinal fluid there will be a diminution of blood, especially in the veins and sinuses because the pressure within them is lower, therefore they yield more readily. If, now, cerebro-spinal fluid be withdrawn then the space it occupied, must be filled by a corresponding increase of blood in the blood vessels, chiefly in the veins and venous sinuses. If much fluid be withdrawn, there will be a great increase in the intracranial blood volume and this will lead to great and sudden engorgement of the vessels within and on the brain and of the membranes and sudden engorgement of the membranes will lead to tension on or bring about a state of oxygen want around the nerve endings within the unyielding *dura*, sufficient to give rise to pain in the manner already described. The time factor in such cases plays an important part in causing pain. The suddenness of the engorgement is the main thing, because great engorgement very gradually produced may not cause pain. It is obvious then that for this reason alone cerebro-spinal fluid should be withdrawn gradually.

In migraine headache is the most important symptom, but from the point of view of getting some understanding of the symptomatology of this disorder it is not the most significant. Migraine often begins not with headache but with sudden numbness over localized areas—the tongue or the lips or the fingers or hand—or it may begin with hemianopsia or scintillating, many-coloured zigzag lines, forming the circumference of the arc of a circle, which are in a constant state of oscillation, or sudden paresis of the hand or arm or a sudden transient disturbance of speech amounting in some cases to motor apraxia. Such symptoms of sudden onset, I think it will be admitted, can be explained only on the ground that the blood supply to certain parts of the brain has been temporarily cut off or greatly diminished, that is that such parts are subjected to a state of oxygen want.

Now, if oxygen want does explain all these other symptoms of migraine, may we not assume that the associated headache has a similar cause and this seems to be confirmed when we reflect that it is one of the outstanding symptoms of oxygen want.

With regard to cerebral tumours, how are we to explain the headache which so frequently accompanies them? A cerebral tumour, like the blood extravasated in a case of cerebral hæmorrhage, occupies a certain space. When there is a cerebral tumour some of the contents of the skull—blood and cerebro-spinal fluid—must have been pressed out from the veins and venous sinuses and subarachnoid space to make room for it. The blood volume is thus diminished and this leads to cerebral anæmia or anoxæmia which in its turn stimulates the vasomotor centre. The result is a general increase of blood pressure and this leads to an increase of intracranial pressure.

Now the intracranial pressure or the pressure of the brain against the cranial wall, is in all physiological conditions the same as the intracranial venous pressure. If it were greater than the intracranial venous pressure the circulation within the cranium would soon cease. The intracranial pressure in the horizontal position is low. According to Leonard Hill it equals about ten millimetres of mercury. In the condition of strychnine poisoning the intracranial pressure may rise to fifty millimetres of mercury. This increase is due to the obstruction of the venous flow into the heart.

In cases of definite arteriosclerosis the blood pressure reaches a greater height than is to be found in cases of cerebral tumour unassociated with vascular degeneration. But in only a small percentage of cases of arteriosclerosis with high blood pressure is there any complaint of headache. Moreover, headache is not present in every case of cerebral tumour. Nor is there necessarily an increase of intracranial pressure in all cases of cerebral tumour. Indeed patients have died as a result of cerebral tumour without the manifestations of those symptoms which would have suggested its existence. Further, when headache is a prominent feature of cerebral tumour, it is not constantly present. It comes and goes. It may be absent for hours or days together. These observations go to show that the headache which accompanies cerebral tumour, is not directly due to the tumour or to increased intracranial pressure, but to some other associated condition.

Now a cerebral tumour cannot exist and continue to grow without interfering with the cerebral circulation. As Leonard Hill states, "room for the new growth can be found only by compensatory

expression of blood or by brain atrophy." Such interference with the circulation will lead to obliteration of some vessels and constriction of others. Hill also writes as follows:

When a local area of capillaries is thus blocked by a foreign body the blood takes the pathway of least resistance through the other vascular areas of the brain. In and around the compressed area, if it be extensive, there lie a large number of arterioles in which the mean arterial pressure is attained, for the outlet from these vessels is blocked. The arterial pressure transmitted from this area through the brain substance will tend to produce compression of other capillary and venous areas. At the same time exudation of fluid at arterial pressure may take place from the blocked vessels and produce œdema of the brain, which in its turn will tend to compress neighbouring capillary areas.

Further:

Cerebral tumours can produce acute attacks of compression by exciting inflammation with hæmorrhages, œdema of the brain substance, thrombosis of the blood vessels and thickening of the meninges.

It is quite obvious, therefore, that the circulatory disturbances produced by cerebral tumours are of profound importance. Briefly, such disturbances lead to obliteration of some vessels, constriction of others and œdema of certain areas of the brain or meninges.

Now, constriction of vessels leads to anæmia of the tissues supplied by them and anæmia implies oxygen want. Likewise in an œdematous area the gaseous exchange between the tissues and the blood is impeded and the tissues will suffer from oxygen want. Further, the anæmic areas and the œdematous areas may be far removed from the site of the tumour. If such anæmic or œdematous areas include certain cells of the *thalamus* or of the sensory cortex or certain nerve endings in the meninges, then there will be produced those very conditions which result in headache and which we have already fully discussed.

Bibliography.

1. J. S. Haldane: "Respiration."
2. A. E. Mills: "Vertigo," Transactions of the Australasian Medical Congress (British Medical Association), First Session, Supplement to THE MEDICAL JOURNAL OF AUSTRALIA, June 14 and 21, 1924, page 429.
3. J. C. Meakins and H. W. Davies: "Respiratory Function in Disease."
4. Leonard Hill: "System of Medicine," Allbutt and Rolleston, Volume VIII, "Diseases of the Brain and Mental Diseases."

Reports of Cases.

RESECTION AND ANASTAMOSIS FOR INTUSSUSCEPTION IN AN INFANT.

By R. H. MACDONALD, M.B., Ch.M. (Sydney),
South Grafton, New South Wales.

Clinical History.

M.E., a female, aged three months and three weeks, breast fed, was admitted to Clarence House at midday on December 5, 1927, with a diagnosis of gastro-enteritis.

The history was as follows. The child had been perfectly well until the afternoon of December 4, 1927, when she apparently suffered suddenly from severe abdominal pain. During the attack the child had cried vigorously. The bowels had functioned freely. During the night the child vomited.

On admission on December 5, 1927, the patient was pale and drowsy. The temperature was 37·5° C. (99·6° F.), the pulse rate 142 and the respiration rate 44 per minute. Nothing abnormal was detected on abdominal examination. The abdomen was soft and no tenderness was elicited. No mass could be detected and the patient was apparently free from pain. A saline solution bowel irrigation was administered and the return contained some blood, but no mucus. The child was hungry, drank albumin water and boiled water thirstily and slept well after drinking.

On December 6, 1927, the general condition appeared to be considerably improved. The patient slept most of the day and took drinks well. The bowels did not function.

In the early hours of December 7, 1927, the child had severe attacks of abdominal pain. During the attacks the legs were drawn up and she screamed lustily. There was absolute constipation and the returns from bowel irrigation contained blood and mucus. A diagnosis of intussusception was made. The child's father was many miles away in the country and many hours were spent in communicating with him before permission for operation could be obtained. During this delay attempts were made to unlock the bowels by saline irrigations administered through a catheter connected to a douche can suspended above the bed. On each occasion blood and mucus appeared in the return, but no trace of fæces was detected.

At this stage the abdomen was slightly distended and in the afternoon a suggestion of a mass could be felt at the right side of the abdomen at the level of the umbilicus. The *signe de dance* was apparent. Nothing was detected on rectal examination, but the finger of the glove was blood stained. Between attacks of pain the child was bright and even smiled.

Eventually permission for operation was obtained and at 8 p.m. on December 7, 1927, a laparotomy was performed. Under open ether anæsthesia an incision was made through the sheath of the right *rectus abdominis*, the centre of the incision being at the level of the umbilicus.

On opening the peritoneum distended coils of ileum presented and with difficulty a large amount of bowel was prevented from escaping. There was a large quantity of free fluid in the peritoneal cavity. The patient collapsed immediately after the peritoneum was opened and the procedure was slightly delayed. Recovery from the initial collapse was slow and incomplete. Camphor in oil, 0·18 mil (three minims), was administered hypodermically and the distended coils of small intestine were packed off. A mass was found in the ascending colon a little above the level of the umbilicus and the diagnosis of intussusception was confirmed. By manipulation reduction was at first easy. The intussusceptum readily retreated through the ileo-caecal valve and the ascending colon caecum and appendix appeared to be perfectly normal. The lack of inflammation of the appendix was particularly striking. Gentle manipulations were continued but at a distance of approximately fifteen centimetres (six inches) from the ileo-caecal junction reduction became difficult. The ileum was dark in patches and lustreless. Soon further reduction became impossible, the intestine being quite gangrenous. It was quickly realized that the only chance of recovery lay in extensive resection and anastamosis. The anæsthetist reported that the radial pulse was not palpable and had not been palpable for some time. The respirations were exceedingly slow and shallow and the colour was very bad. A further 0·18 mil of camphor in oil was injected and resection was proceeded with as quickly as possible. It was considered safer to remove all intestine of low vitality as well as the patently gangrenous portion. The ileum was divided between clamps both proximally and distally to the unreduced mass. The divided ends were closed and invaginated. The mesentery was clamped, divided and ligatured. The distal portion of ileum remaining measured approximately fifteen centimetres (six inches) from the closed end to the ileo-caecal junction. The proximal and distal portions of the ileum were approximated and a lateral anastamosis performed. The suturing was done in two layers with fine plain catgut. The communicating aperture was of sufficient size to admit two fingers easily when completed.

The infant's condition was parlous, but the suggestion of introducing saline solution into the peritoneal cavity was vetoed for fear of spreading infection. The omentum was brought to the site of the anastamosis, but was not sutured thereto and a soft rubber drain was introduced into the peritoneal cavity. The abdomen was closed in layers round the tube, plain catgut being used throughout with four silk worm retaining sutures.

At the end of the operation no radial pulse could be detected. The infant was detained on the table with the head lowered while subcutaneous saline solution to the amount of one and a half litres (two and a half pints) was given. On account of the shock and restlessness after return to bed a hypodermic injection of morphine, 0·54 milligramme (one one hundred and twentieth of a grain), was administered. The condition gradually improved through the night up till 7 a.m. on December 8, 1927, when the child suddenly collapsed. An injection of 0·06 mil (one minim) of camphor in oil was given followed immediately by the same quantity of a one in a thousand solution of adrenalin. The recovery from the collapse was dramatic, the radial pulse returning within a few minutes.

At 4 p.m. on December 8, 1927, some fæces were passed naturally. The drainage tube was removed at the end of twenty-four hours. Fluid was taken through a gauze swab held in forceps on December 8, 1927, and diluted breast milk on December 9, 1927. On December 10, 1927, undiluted breast milk was taken from the spoon and the child was put to the breast a few days later. Convalescence was uneventful, fæces being passed from three to four times a day. The patient was discharged on December 24, 1927, the condition being exceedingly good. The infant had put on 0·22 kilogram (half a pound) weight since the operation. On December 29, 1927, the weight had increased a further 0·22 kilogram and on January 14, 1928, the weight had increased another 1·1 kilogram (two and a half pounds).

Comment.

It was considered that this case was worthy of report on account of the apparent infrequency of infants under the age of twelve months surviving a resection and anastamosis.

Clubbe[1] in 1921 had collected the reports of sixteen cases of recovery after resection for intussusception in children. The ages varied from five days (Dowd) to four years.

Moynihan[2] quotes in a table of results of 399 cases of intussusception 29 cases of resection and anastamosis with nine recoveries. This table was prepared by Perrin and Lindsay from the records of the London Hospital over a period of eighteen years. The nine patients who recovered were all over the age of three years. There were no other recoveries in children from irreducible intussusception treated by different methods. He also gives the statistics of the Leeds General Infirmary from 1915 to 1924 in which there were 29 cases of resection with three recoveries. The ages of the three children who recovered, were respectively one year, six months and three months.

Romanis and Mitchener[3] are very pessimistic on the subject and after detailing the various methods of dealing with an irreducible intussusception even go so far as to write:

> As a certain number of cases undoubtedly undergo spontaneous cure by the intussusceptum sloughing and passing, the chances of this occurring are rather greater than the chance of a baby under a year old surviving any of the above procedures. If the intussusception is irreducible in a tiny child it is probably therefore better to leave it and close the abdomen.

Makins[4] favours the Jesset-Barker operation for irreducible intussusception. He quotes results by von Eiselsberg who recorded nine recoveries in twelve cases of ordinary intussusception treated by excision, but writes: "These results are not comparable with those of resection performed for gangrene or in toxæmic patients."

This author gives the results of resections performed at Saint Thomas' Hospital from 1888 to 1908. The results over this period were not encouraging. In twelve cases of resection with immediate union only two adults survived and in fifteen cases of enterostomy alone or enterostomy combined with excision there were no recoveries.

That the recent results have been more encouraging would appear from a report on the discussion of a paper read by Mr. Alexander McLennan[5] at the annual meeting of the British Medical Association at Edinburgh in 1927. By two surgeons present six successful cases were described.

Undoubtedly there have been many other cases unrecorded, but while opinions like that expressed by Romanis and Mitchener[3] continue to appear in modern textbooks, it seems important that successful cases should be published.

The reporting of this case involves a confession on the part of the writer of having been deceived in the early stages of the illness by the appearance of the infant, the results of physical examination and the patient's apparent freedom from pain.

I have come to the conclusion that the enteric intussusception occurred at the onset of the illness and the pains on December 7, 1927, occurred when the already existing, more or less chronic, intussusception entered the colon and the mass was first appreciated. As the child was admitted during an epidemic of acute gastro-enteritis, two of my colleagues have been sufficiently charitable to assure me that the condition was undoubtedly one of acute intussusception superimposed on an acute gastro-enteritis. I cannot convince myself, however, that considerably more than a foot of ileum could have become gangrenous in the time between the onset of the second series of pain and the laparotomy.

Acknowledgements.

In conclusion, my sincerest thanks are offered to Dr. W. Roy Wilson, of Grafton, for his great patience and skill in administering a difficult anæsthetic, to my partner, Dr. W. K. Muston, for his very able assistance which was instrumental in reducing the time factor to a minimum and to the Matron, Miss K. Sinclair, and her staff, who were responsible for steering the little patient safely through the stormy stage of her convalescence.

References.

(1) Charles P. B. Clubbe: "The Diagnosis and Treatment of Intussusception," Second Edition, 1921, pages 63 and 77.

(2) Berkeley Moynihan: "Abdominal Operations," Fourth Edition, 1926, Volume II, pages 148 to 154.

(3) W. H. C. Romanis and Phillip H. Mitchener: "The Science and Practice of Surgery," 1927, Volume II, pages 650 *et sequelæ*.

(4) G. H. Makins: "Oxford Surgery," 1919, Volume II, pages 814 to 820.

(5) Alexander McLennan: "Acute Intestinal Obstruction in Infancy and Childhood," *The British Medical Journal*, November 5, 1927, page 818.

Reviews.

A BEGINNER'S GUIDE TO PRACTICE.

THERE is, as we have all learned by most bitter experience, a vast difference between hospital and private practice. The student and hospital resident find medicine a very fascinating and moderately straight forward affair, but after a few days in general practice they find themselves adrift with little in their previous experience to help them. To a great difference in the class of work they are called upon to do is added the overwhelming fact that medicine has become a livelihood and not a vocation.

It is to help them in their early struggles that Dr. Stanley Sykes, a former house-surgeon of Saint Bartholomew's Hospital and now a general practitioner in

Yorkshire, has written a very helpful little book.[1] In fact, it is too little; its chief defect is that it could be made twice the size and still much that is of value would necessarily be omitted, but its size gives it two excellent qualities for the young practitioner: it is easy to read and it is cheap.

He begins at once by discussing visits, how often to visit, *locums*, death certificates and then slides on into a discussion of the position of general practice. In this he writes a spirited defence of the general practitioner and shows himself as a man well able to appreciate both sides of the question.

Then follows a chapter on patients, their sayings, doings and idiosyncrasies and in spite of the difference in temperament between Australians and Yorkshiremen, he writes much of interest to a young practitioner in this country.

He deals with the diseases of general practice and it is interesting to find that he puts influenza first, next appendicitis, then "other diseases" and finally diphtheria. In this last he had very bad results, four deaths among sixteen patients, one from laryngeal blockage and three from heart failure. From other passages it is probable that they were seen late in the disease, so that the result is not to be wondered at, considering his miserably inadequate doses of antitoxin, eight thousand and six thousand units. It is curious, too, that there is no suggestion that diphtheria is a hospital disease. To attempt to treat it at home in a working class neighbourhood would be looked on as criminal folly in this country. He gives a list of the diseases he has met with in his practice. Influenza heads the list with 335, measles with 92 shows that there is a considerable proportion of children in the practice, as does chicken-pox twenty, but no mention is made of infantile diarrhœa in any form.

To an Australian this is quite incomprehensible. It is the more remarkable in that he gives some very sound directions for handling children in examination and treatment.

His chapter on prognosis seems to point to its difficulties. He deplores the lack of opportunity the resident medical officer in hospital has to make a prognosis or to undertake that even more difficult problem, the treatment of prolonged and inevitably fatal conditions.

Is it this ignorance and the attitude of impatience which it sometimes produces, that drives so many hopeless patients to the quack? The experienced charlatan at least promises much and does something, though this something may produce neither alleviation nor cure.

A chapter on dispensing drugs will make us glad that dispensing is not a common part of medical practice in this country.

There is an excellent chapter on instruments and equipment in which, however, the author omits a most valuable part of the physician's equipment, "a convulsions bag," with everything ready packed for dealing with a patient in convulsions at a moment's notice.

Two chapters on certificates and official forms (there are thirty-four of them) and on insurance practice make us realize the joys of active State-controlled medicine. It is probable that medical practice under an insurance scheme with medical benefit is a much more efficient and pleasant service than under the old club *régime*. The emasculated form of national insurance about to be introduced in Australia is quite another matter. These chapters should be read most carefully by every Australian practitioner who would like to realize something of the human side of panel practice.

In dealing with midwifery (and the writer is an ex-assistant obstetrician of his hospital) he takes up the cudgels vehemently on behalf of the much maligned general practitioner and invites the obstetrical pundits to produce as good results as the general practitioner is getting in the conditions in which he has to work. At the same time he recognizes how bad these conditions are (quite unrealizable by most Australians) and welcomes the establishment of maternity homes by the local authorities.

Two chapters on anæsthetics are full of interest, but though a champion of ethyl chloride (he considers it nearly as safe as nitrous oxide) he does not administer it by the open method except to children under three years, possibly because of expense. In the opinion of many surgeons the simplicity, comfort and safety of the open method for patients of all ages places it far above the inhale methods. He describes the ethyl chloride-ether sequence by the open method very well as an excellent method for children only. This limitation is surely unwise. There is a very suggestive passage on chloroform in obstetrics.

The author concludes his book with a short chapter on venereal disease and especially the vexed question of prevalence. The Royal Commission of 1916 gave 10% for the incidence of syphilis among the general population. Dr. Sykes from his own practice gives the incidence of syphilis as 0·22% and that of gonorrhœa as 0·71%. The figures may represent the incidence of venereal diseases in the confines of the author's Yorkshire practice, but they do not serve any useful purpose, since they have no counterpart in the general community. Unfortunately both syphilis and gonorrhœa are terribly common in all so-called civilized communities.

The book is essentially one to read and enjoy with a keen liking for the author and a hope for more from his pen.

[1] "A Manual of General Medicine Practice," by W. Stanley Sykes, M.A., M.B., B.Ch. (Cantab.), D.P.H. (Leeds), M.R.C.S., L.R.C.P.; 1927. London: H. K. Lewis and Company, Limited. Crown 8vo., pp. 228. Price: 7s. 6d. net.

THE VALUE OF VACCINATION.

"TO WHOM IT MAY CONCERN"[1] is a model address warning the public against the risks of small pox and advocating vaccination with the force of so recognized and experienced an authority as Dr. Wanklyn, Medical Consultant of the London, Middlesex, Essex and other County Councils.

Descriptions of actual cases picture vividly the loathsome appearance and dread effects of this disease.

With regard to the milder form of small pox, such as Sydney experienced in 1913, we are warned that the fact of the prevalence of the milder form is a standing and certain index of how vulnerable we are to the severer form. A fact of great interest to Australia is that the main attack of small pox is constantly from the East.

There is an immense quantity of small pox always infecting the world in nearly every part. In 1918 there were 93,000 recorded deaths in British India. It is estimated that there are sometimes more than 1,000,000 cases in the world every year. Obviously offshoots from this mass of infection must continually find their way to us in our traffic from overseas.

The author shows graphically what it means suddenly to be faced with a case of small pox in an unvaccinated community. He instances the case of a hospital where some of the nurses were unprotected and relates that the gentleman in lay charge of the hospital who had been grievously misled by anti-vaccination propaganda, revised his opinion: "when that bonny nurse was taken ill and died with small pox, it was then that small pox knocked at my door."

A practitioner went into a small pox ward and saw on the beds around him twenty or thirty patients all lying in different stages of this horrible disease and yet moving about among them a number of trim, healthy looking nurses and doctors, all in perfect fitness and composure. The contrast was so amazing that he was compelled to ask himself in what that immunity consisted. In their having been properly vaccinated, of course.

Although of the nature of propaganda this work is valuable also to the medical officer as summarizing the necessary steps to check the spread of the disease. In view of our vulnerable position in Australia with a susceptible and unprotected people, an address such as this would be invaluable especially in the event of small pox penetrating the quarantine barrier.

[1] "To Whom it May Concern: A Popular Address About Smallpox and Vaccination," by Wanklyn, B.A. (Cantab.), M.R.C.S., L.R.C.P., D.P.H.; London: The Voluntary Service Fund. Demy 8vo., pp. 34. Price: 1s. 6d. net.

The Medical Journal of Australia

SATURDAY, FEBRUARY 11, 1928.

A Retrospect.

Physiology.

THERE has been steady progress in many directions in physiology during the year 1927, although there have been no discoveries of unusual merit.

The ethyl chloride method devised by Yandall Henderson and Haggard for determining the output of the heart gave hopes that more information would be obtained by its means concerning the functional activity of the heart under varying conditions. There have been several severe criticisms of the method. At the present time it must be admitted that no satisfactory method for the determination of the output of the heart under physiological or pathological conditions is in existence. The chemical basis of the method has been attacked by several workers, both on account of the figure accepted as the coefficient of absorption of ethyl chloride in blood plasma and its destruction in the body and on account of the methods employed in the quantitative estimation of the expired air. H. Barcroft has shown that several factors may influence the figures obtained. The circulation rate estimated in this manner may be 20% or even 30% too high. In addition it has been shown that under normal conditions the capillaries and alveoli may be closed; under pathological conditions they certainly will be closed. In consequence the apparent circulation rate may be too small by an unknown and indefinite amount.

The opinion has been held that during exercise the diastolic size of the heart is increased. F. D. McCrea has recently carried out some work with the result that he challenges this teaching. He has shown by means of teleskiagrams that moderate exercise is characterized by little or no change in the diastolic volume. During severe exercise there was evidence of some increase in the size of the heart, but the volume changes were small. A slight decrease in size was observed after heavy exercise. Venous pressure did not tend to rise when the pulse rate was high and the cardiac volume also did not increase. When the pulse rate was slow, the venous pressure was usually high and the diastolic size of the heart tended to increase.

The relation of histamine and bodies behaving like histamine to physiological activity has been the subject of some interesting investigations. T. Lewis and others have adduced much evidence in recent times that minor injuries to the skin, such as light scratches, wheals and so forth, are associated with the liberation in the skin of small amounts of substances indistinguishable from histamine. They also showed that flushing occurring from antidromic changes and *herpes zoster* are caused by the conveyance of impulses along the sensory nerves not to the vessels but to the tissues of the skin. These impulses release the histamine-like substances in the skin and thus give rise to vasodilation in the area of release as a result of the action on the minute vessels. C. H. Best, H. H. Dale and W. V. Thorpe have demonstrated that histamine is present in tissues which have been subjected to the smallest amount of destructive change at the time of death. They have arrived at the conclusion that histamine is present as such in living cells or is liberated from some constituent in the cells at the moment of death. The lung appears to be particularly rich in histamine. They claim that this cannot be without significance.

The most important publication dealing with the ductless glands is that of Harrington on thyroxin. After a brilliant piece of research into the constitution of thyroxin, in the course of which he proved that it is an iodine derivative of tyrosin and not of indol, as Kendall maintained, he crowned his effort by a particularly fine synthesis of thyroxin.

C. S. Hicks has demonstrated that thyreo-globulin passes from the thyreoid to both lymphatics and veins, chiefly the latter. Stimulation of the sympathetic nerve supply to the thyreoid gland produces no change in the secretion of thyreo-globulin. The administration of iodine appears to increase the flow of lymph from the gland and the thyreo-globulin content of the lymph.

Hindmarsh has determined the basal metabolic rate of Sydney students and finds that the men

have a rate averaging 8·9% below the predicted value according to Du Bois and the women a rate averaging 10·5% below the predicted value. She suggests that the reduced rate is caused by the increased muscular relaxation of persons in the warm climate of Sydney.

Bacteriology and Immunology.

Some highly important and a great deal of useful work has been recorded in the past year. The doctrine of the bacteriophage originated by d'Herelle has led to further researches in many laboratories. It is certain that the full importance of this work has not yet been demonstrated. Carl Prausnitz has found that he has experimental evidence of a variability of different kinds of bacteriophage. He maintains that it is possible to accustom the bacteriophage to the noxious effects of certain disinfectants. He agrees with d'Herelle that the bacteriophage is a living organism.

J. A. Arkwright has studied the antigenic properties of the members of the enteric-coli group. He holds that the distinction of so-called rough and smooth colonies is of significance. He regards the smooth colony as the normal condition, while the rough colony is a variant. The former are composed of highly virulent bacteria which are resistant to the action of heat. Since their antigenic properties are greater than that of the modified bacteria of the rough colonies, the former should be employed for the preparation of prophylactic vaccines. They confer a greater degree of immunity. The serum of a well immunized person is found to contain agglutinins.

The subject of the pathogenesis of scarlet fever is still claiming attention. Griffith has found that hæmolytic streptococci isolated from patients with scarlet fever can be divided into three main serological groups and one large fourth group of heterogeneous organisms. Group II is well defined and this group has not been found in association with any disease other than scarlet fever. Gunn has attempted to correlate the type of coccus with the clinical findings. Group I was isolated on rare occasions. Group II was recovered from persons with the most typical and severest forms of the disease. The severity of the attack was less in those patients from whom Group III was gained. It appears as if Group IV is usually associated with mild infections. Similarly the complications were found to be severe in Group II infections and less numerous and milder in those attacks associated with Groups III and IV.

In their experiments to determine the value of active immunization of susceptible individuals against scarlet fever Benson and Simpson have found that injections of toxin of hæmolytic streptococci at intervals of from five to fourteen days in gradually increasing doses render the majority of those who react to the Dick test, no longer able to do so. The immunity lasts for a few months. If more lasting immunity is required, much larger doses than those usually used are necessary.

W. H. Park has introduced a modification of the Schick test for diphtheria. He injects one cubic centimetre of a standard preparation of toxin-antitoxin mixture subcutaneously. He states that while this injection reveals the presence of susceptibility, it also serves as an immunizing agent. Children under the age of five years are usually susceptible; Park considers that it is unnecessary to subject them to the Schick test. He gives them three injections of toxin-antitoxin mixture needed for immunization.

A. N. Kingsbury has attempted to control an epidemic of morbilli in the Federated Malay States. He found that three and a half cubic centimetres of serum of persons convalescent from an attack protected a large proportion of those exposed to infection and modified the attack in those who were not completely protected.

Some additional information in regard to the pneumococci has been published. A large series of patients suffering from pneumonia has been studied. It was found that infections with Types II and III were the most fatal and Types I and IV were the mildest. Young people appear to be more prone to infection with Type I and elderly people to infection with Type III. Severe complications were encountered in the Type I infections.

A new principle has been enunciated in connexion with the preparation of gonoccoccus vaccines. Lambkin, Dimond and Robertson found that the antigenic properties of gonococci are confined to

polar bodies which appear when the organism is grown on media rich in nucleo-protein. These polar bodies can be separated from the cocci by the action of a 2% solution of sodium chloride. They recommend a standardized solution of the nucleo-protein of 100,000 million gonococci in fifteen cubic centimetres of 2% saline solution for intraurethral injection.

N. Hamilton Fairley and F. Eleanor Williams have described a new intradermal test in schistosomiasis. The antigen is derived from the dried powdered livers of snails infected with bilharzial *cercariæ*. The test is diagnostic, but does not afford an index of the effect of treatment.

Harold R. Dew has continued his researches on hydatid disease and has collected all the evidence concerning the production of hydatid anaphylaxis.

R. W. Cilento, T. C. Backhouse and G. M. Heydon have recorded the first case of paragonimiasis in New Guinea. This disease is said to be endemic in Japan, Formosa, Indo-China, India and Peru and enzootic in parts of the United States of America and in Venezuela. No case has been recorded in Australia. Heydon has identified the parasite as *Paragonimus ringeri*.

F. S. Hone and W. S. McGillivray have published further information concerning the occurrence of modified typhus fever in Australia. There is no longer any doubt concerning the nature of the infection. Hone's contribution is an admirable summary of all that is known of this peculiar form of disease.

At the second session of the Australasian Medical Congress (British Medical Association), held in Dunedin in February, 1927, Jean Macnamara and F. G. Morgan gave an excellent account of the method adopted in the collection and application of immune serum in the treatment of poliomyelitis.

The confusion that has arisen in the course of time in regard to spirochætal jaundice has been cleared up to a large extent by a painstaking investigation by G. Buchanan. He has paid attention to the ætiological factors, including the behaviour of the causal organism, the *Leptospira icterohæmorrhagicæ*, the diagnosis and differential diagnosis, the mortality and the pathology of the jaundice.

Current Comment.

THE PREVENTION OF DIPHTHERIA.

THE tragic accidents that occurred to twelve children of ages varying from two to seven years in Bundaberg on January 28, 1928, have caused much uneasiness throughout the Commonwealth. Deep sympathy is felt with the parents of the twelve healthy children who have lost their lives as a result of a plan of prevention of disease. That the occurrence has but little real significance in connexion with the control of diphtheria must be admitted in view of the history of toxin-antitoxin immunization. Accidents have taken place on a few occasions in the past. The number of deaths due to faulty technique, improper mixing and unforeseen biological reactions is certainly less than forty. Up to 1926, over two million injections of toxin-antitoxin were given in New York alone without a single mishap. It is safe to assume that since 1913 when Schick introduced the test for susceptibility known by his name and von Behring employed a toxin-antitoxin mixture for the purpose of immunizing human beings against diphtheria, not less than one and a half million children and adults have been immunized. From the experience in New York alone Schick testing and the immunization of susceptible children has reduced the death rate from diphtheria from 22·7 per 100,000 to 7·9 per 100,000. In other words the immunizing of approximately 400,000 children in eight years has had the effect of saving over 2,750 lives. The chief campaigns have been conducted in large cities. Much has been effected in America and England and Scotland and much more will be gained in the next few years. The total saving in life, large though it undoubtedly is up to the present, does not represent the whole gain. Schick testing and the immunization of susceptible children has had an undeniable effect in reducing the number of infections. Had the incidence of the disease remained at the 1917 level in New York, the number of persons attacked would have been increased by approximately 19,000. It is the aim of Dr. W. H. Park to increase the number of immunized children in New York to 1,800,000 by the end of 1930. Provided that the effect is maintained at the same rate as obtained up to the end of 1926, the saving of infections would amount to about 85,500 and the saving of lives would be equal to about 12,350. From these figures it will be seen that the prevention of diphtheria by means of immunization throughout the world has already been of very great value.

In order that the problem may be seen in proper perspective it is necessary to remind the reader of certain facts, some of which are well known, some of which are not generally recognized.

The causative organism of diphtheria was discovered by Klebs and Löffler in 1884. Prior to this date it was recognized that diphtheria was a specific infection depending on some living virus. Bretonneau had established its specific nature beyond all doubt sixty-three years previously. The discovery of the bacillus and the ease with which

it can be cultured on serum rendered possible the definite diagnosis of an infection within relatively few hours. In the year 1890 Tizzoni and Cattani demonstrated that dogs could be immunized against tetanus by the injection of the filtrates of cultures of tetanus bacilli and that the serum of the immunized dogs conferred a protection against the disease in susceptible animals. In the same years von Behring and Kitasato proved that the serum of animals immunized against diphtheria or tetanus was not bactericidal but was antitoxic. This discovery was seen at once to be of immense clinical importance. It took five years before methods for the immunization of horses with the filtrates of broth cultures of diphtheria bacilli were sufficiently elaborated for practical purposes. In 1895 antitoxin was available in Europe for trial and a careful, properly controlled test was carried out at the Eastern Hospital, Metropolitan Asylums Board, in the north-east of London. The results were so extraordinary that antitoxin was used as the standard treatment of diphtheria in all institutions in England within a few months of the issuing of the preliminary report. Within two years it was found that antitoxin was capable of reducing diphtheria mortality almost to zero provided that a sufficient dose was administered on the first day of the disease. The mortality was found to rise rapidly as the period between the onset of the illness and the application of the remedy increased. When antitoxin was injected on the fifth day or later, the mortality was as high as it was in untreated children. At first the concentration of the antitoxin, calculated as units per cubic centimetre, was low. About a fortnight after the injections severe serum rashes appeared and were accompanied by fever and profound illness of short duration. At times this serum sickness was fatal. The first clear account of this side effect of antitoxic serum was published by von Pirquet and Schick in 1905. Two years before Richet had called attention to the artificial increase in the toxicity of actines to dogs which had previously received injections of extracts of the tentacles. At a later date Richet gave this phenomenon the name of anaphylaxis. About 1906 Rosenau and Anderson, Otto and others working with antitoxin and other forms of horse serum noted that guinea pigs often died suddenly with characteristic symptoms when a small injection of horse serum had been given at least ten days before a second and larger dose. During the course of the following four years many observations were recorded in connexion with this phenomenon. It was possible to establish the state of hypersensibility or anaphylaxis by sensitizing with a minute dose of protein. The condition was specific and the test dose had to be of the same or an allied protein. It is not necessary to refer to Arthus's phenomenon and to Theobald Smith's phenomenon in this place. Soon it became evident that the serum sickness of von Pirquet and Schick was an anaphylactic condition, but that human beings did not behave like guinea pigs when exposed to the shock. As it became clear that repeated injections of serum were accompanied by grave danger of an acute shock, the subject of anaphylaxis attracted a large number of workers who endeavoured to determine the nature of the phenomenon and to define the conditions under which antianaphylaxis could be established. In spite of the grave fears of fatal accidents resulting from the repeated injection of serum, the experience of a third of a century has taught that death from anaphylaxis induced in human beings by the injection of diphtheria antitoxin does not occur. It must be remembered that antitoxin is given to a large proportion of persons suffering from diphtheria, that the incidence of diphtheria during the thirty-three years has not been less than 2% of population in England and Wales, which would represent about two and a quarter million infections. A conservative estimate would be that over one million persons received injections of antitoxin in England and Wales alone since it was introduced. The number of injections given in the period throughout the whole world must be many millions. If anaphylaxis were a real danger, the treatment would have fallen into disrepute long ago.

So much for the safety or otherwise of the antitoxin fraction. It goes without saying that diphtheria toxin is a deadly poison. Under ordinary circumstances the toxin is diluted for testing purposes until one-tenth of a unit or lethal dose is contained in one cubic centimetre. The lethal dose is the amount of toxin sufficient to kill a guinea pig weighing two hundred and fifty grammes in four or five days. For the Schick test a quarter of a cubic centimetre is injected into the skin. This dose is quite harmless to a child, even if injected under the skin instead of into it. For immunizing purposes the initial dose is usually 0·125 cubic centimetre of a mixture of toxin and antitoxin and this is increased to 0·5 cubic centimetre and one cubic centimetre in the two succeeding doses. The ordinary lethal dose of toxin is about 0·028 cubic centimetre. A very large amount of work has been carried out in connexion with the neutralization of the toxin or combination of the toxin and antitoxin. For our present purpose it is unnecessary to enter upon a discussion of the several hypotheses and arguments put forward regarding this matter. Toxin-antitoxin mixture contains the quantity of the latter necessary to prevent the death of a guinea pig from the effect of toxin. In the early days Ehrlich found that it was advisable to define standard units of toxin, antitoxin, L_o and L_+ values. The antitoxin unit is the amount of antitoxin required to neutralize one hundred lethal doses of toxin. L_o signifies the maximum amount of toxin that can be given with one unit of antitoxin to a guinea pig weighing 250 grammes without the production of a general or local reaction. L_+ means the amount of toxin that is needed to kill a guinea pig weighing 250 grammes when injected with one unit of antitoxin. Ehrlich observed that the difference between L_o and L_+ measured as minimum lethal dose was very much larger than could be accounted for by a simple calculation. It thus appears that complete neutralization with antitoxin of the toxin is essential for immunization purposes. The actual magnitude or measure of the toxin in the broth

filtrate cannot be determined, but it is obviously extremely minute. The antitoxin content of serum is also at present imponderable. It is always attached to the globulin of the serum and apparently behaves like an enzyme. It is probable that antitoxin is not a chemical entity, but a property of globulin with an altered molecular arrangement. It has been noted that if the amount of antitoxin or rather antitoxic serum be insufficient to neutralize the toxin, instead of the former neutralizing a definite amount of toxin, it is distributed equally through the whole mass of toxin. In other words there is partial absorption. Whether the combination is a chemical one or merely a physical blockage has not been definitely determined. The toxin is not destroyed by the attachment of the antitoxin, for it is possible to disconnect the parts and to free the toxin from the restraining influence of the antitoxin. Moreover, even when the combination is undisturbed, the toxin can exert its power as an antigen.

Toxin that has deteriorated by standing, exposure to heat and other physical influences, loses its poisonous effect and is known as toxoid. Ehrlich held that toxin, toxoid and toxon existed side by side as allied but separate substances. This view is probably incorrect. Toxoid or deteriorated toxin seems to have an affinity for antitoxin but slightly less than that possessed by toxin. In England the employment of toxoid-antitoxin mixture for diphtheria immunization is preferred to the usual toxin-antitoxin mixture. In America toxin is still used and the belief is held that it has a more powerful antigenic action.

It has been pointed out that in the course of prophylactic immunization against diphtheria accidents have occurred and the death of a few healthy children has taken place. The known causes of accident may be divided into three groups. Danysz described a phenomenon which has led to disaster in the past. This accident is unlikely to arise in the future. He found that if the quantity of toxin needed to make the toxin-antitoxin mixture is added in two parts and an interval elapses between the addition of the first and the second moiety, the toxin remains incompletely neutralized. It would seem that this failure of equal absorption of toxin is caused by a change in the surface tension of the toxin. Similar phenomena have been studied with other colloidal substances. When the toxin-antitoxin mixture is carefully and skilfully prepared, as it is at the Commonwealth Serum Laboratories, such an accident cannot take place. That this is not the cause of the accidents at Bundaberg is proved by the fact that many children received injections of the same mixture up to a few days of the tragedy without suffering any harm. Similarly, the addition of too little antitoxin can be excluded on the same grounds. This disposes of the first group of causes, the errors in technique in the preparation. The second group comprises the changes that may take place in the mixture after it has been distributed. It has been shown that the combination is split up under the influence of cold. In February, 1924, a batch of toxin-antitoxin mixture was put up in tubes and distributed throughout the United States of America. Some tubes were frozen at Concord and at Bridgwater, Massachusetts, and subsequently thawed before use. Very severe reactions took place in upwards of forty children. The tubes of the same batch that had not been frozen, gave rise to no unusual reactions. It is conceivable that prolonged storage at low temperatures might dissociate the mixture to such an extent that the mixture would acquire highly toxic properties. Although no records exist of an accident due to the alteration of the surface tension by chemical means, it is probable that the addition of certain electrolytes would have the effect of splitting off the toxin from the combination. The mixture, if stored in bulk or in large bottles, may become contaminated with pathogenic bacteria. It is usual to seal the tubes or bottles with rubber stoppers or caps. The needle is passed through the rubber and the mixture is drawn up into the attached syringe. Unless special precautions are taken, this process may lead to contamination of the liquid after the needle has been introduced several times. A tube cannot be opened without grave risk especially in a warm, moist atmosphere, unless this is done in a current of sterile air. In connexion with this accident, it should be remembered that a group of children might become infected from some outside source and those whose resistance has been temporarily disturbed by the reaction of the toxin-antitoxin mixture, might suffer much more severely than children in normal condition. It would be easy to ascertain whether an infection were prevalent in the neighbourhood in such circumstances. The third group of causes is theoretical rather than actual. Although millions of doses spaced in accordance with the plan of active immunization have been given in all parts of the world without accident, it is conceivable that the early injections might render the children hypersensitive and a later dose might invoke an anaphylactic shock. That this did not occur in Bundaberg is certain. In the first place the experience of a third of a century with antitoxin reveals that death from anaphylaxis after repeated injections of antitoxin does not occur, notwithstanding the fears entertained at the end of last century. In the second place the described clinical symptoms and signs are not those of typical anaphylactic shock. Lastly, such an extraordinary accident would not affect as many as twelve children.

From the foregoing it will be gathered that Schick testing and prophylactic immunization of susceptible children is a safe procedure, although want of caution or lack of knowledge has led to disaster on rare occasions. The number of lives saved is overwhelmingly great as compared with the number of lives lost by accident. No sensible person would permit this very sad occurrence at Bundaberg to interfere with the campaign to eliminate diphtheria by the protective immunization of susceptible children in the presence of outbreaks. The cause of accident can be ascertained and can be eliminated.

Abstracts from Current Medical Literature.

PHYSIOLOGY.

The Size of the Spleen.

J. BARCROFT AND J. G. STEPHENS (*Journal of Physiology*, October, 1927) have studied the functions of the spleen by a new method. In their earlier experiments they placed a celluloid window over the spleen and were able to observe changes in the shape and size of the spleen through this. This method gave fairly satisfactory results for about a fortnight. Later they made the spleen extracutaneous and as such it has been kept under observation for more than eight months. Both methods show that the spleen contracts to about one-half to one-third of its size on exercise and to an even smaller volume on death or severe hæmorrhage. The amount of blood squeezed out during exercise is estimated at its maximum as forming one-fifth of the volume of blood in circulation; under such circumstances the spleen becomes pale. These alterations in size depend on the integrity of the nervous supply to the spleen. Psychological processes calculated to culminate in violence may also cause the spleen to pale and contract somewhat, thus anticipating actual exercise. In any case the contraction of the spleen is an early event both in exercise and hæmorrhage rather than a last resort for the acquisition of blood.

The Significance of the Respiratory Quotient.

E. P. CATHCART AND J. MARKOWITZ (*Journal of Physiology*, September, 1927) criticize the significance usually attributed to the respiratory quotient. To many workers the carbon dioxide: oxygen ratio is believed to be sound evidence of the nature of the combustion processes taking place in the organism at the time of the determination. The authors have determined the effects on the respiratory quotient of the ingestion of various sugars. They find that the administration of fifty grammes of glucose causes a leisurely rise of the respiratory quotient, whereas the administration of equivalent quantities of sucrose, galactose, lævulose and dihydroxyacetone brings about a prompt rise in the respiratory quotient to over unity. These differences cannot be attributed to differences in the rate of absorption as is shown by blood sugar estimations. These respiratory quotients cannot be interpreted as indicating a preferential combustion of sugar other than glucose, since the tissues cannot use dihydroxyacetone until this substance has been converted into glucose by the liver. They criticize the conception that the respiratory quotient is solely or even mainly a combustion quotient and make the suggestion that the non-protein respiratory quotient represents not a combustion quotient, but the algebraical sum of the transformation carbohydrate to fat and fat to carbohydrate, *plus* the oxidation of carbohydrate for energy purposes.

Basal Metabolic Rate of Sydney Students.

E. M. HINDMARSH (*The Australian Journal of Experimental Biology and Medical Science*, December, 1927) has made a study of the basal metabolic rate of 76 students of the University of Sydney. She found an average reduction of 8·9% for the men and 10·5% for the women when compared with the Du Bois predicted values. She suggests that the reduced basal metabolic rate is due to the more ready muscular relaxation of the subjects in the warmer climate of Sydney. Subjects who are accustomed to basal metabolic experiments show a much lower rate than untrained subjects, probably due to a better muscular relaxation and the suggestion is that subjects in a warm climate acquire the ability to relax the muscles much more readily without training than do subjects in a colder climate. She has also critically examined the different methods of determining the basal metabolic rate and arrives at the conclusion that the collection of the whole of the expired air for a period of 14·4 minutes with estimation of the carbon dioxide and oxygen gives more consistent results than either the determination of oxygen absorbed or of carbon dioxide excreted alone. The determination of the respiratory quotient and of the volume of expired air acts as a useful check on the normal breathing of subjects. With abnormal breathing very erroneous results may be obtained. Determinations of alveolar carbon dioxide and oxygen immediately before and immediately after the test give the most accurate information of the normality of the sample collected. With abnormal breathing the carbon dioxide method readily gives excessively high results.

The Circulation Rate in Man.

SAMSON WRIGHT AND M. KREMER (*Journal of Physiology*, November, 1927) have made a critical examination of the Henderson ethyl iodide method for the estimation of the circulation rate in man. They find that there are several errors in the arguments of Henderson and Haggard which militate considerably against the accuracy of the method. The partition coefficient of ethyl iodide between air and blood which Henderson and Haggard took as two, they find to vary between two and seven. There is also a considerable return of ethyl iodide in the venous blood when high concentrations are breathed and a definite return when low concentrations are used. Any increase in the circulation rate, general or local, would probably tend to cause a greater return in the venous blood. The ethyl iodide method appears to be unsuitable for determinations of the output of the heart during exercise even for comparative purposes.

Digestion and Absorption of Fat.

THE accepted hypothesis for the absorption of fat from the alimentary canal assumes: (i) that fat is taken into the columnar cells of the villus as fatty acid and glycerol, (ii) that resynthesis of fat occurs in these cells and (iii) that neutral fat passes from the cell into the villus spaces and thence into the central lacteal. J. Mellanby (*Journal of Physiology*, October, 1927) has reinvestigated this question in the cat. The experiments indicate that fat does not require to be hydrolysed into fatty acid and glycerol by lipase before intestinal absorption takes place. The amount of lipase in the cat's pancreatic juice is very small and examination of the alimentary tract shows that there is no additional source of lipase. Emulsified fat placed in the duodenum is not absorbed, but if bile be added to the emulsified fat there is rapid absorption of fat into the lacteals, secretion of pancreatic juice and an increased flow of bile. Possibly the main function of the lipase of pancreatic juice is to hydrolyse a small quantity of fat into fatty acid and glycerol and the soap formed by the neutralization of this fatty acid by the alkali of the pancreatic juice facilitates the formation of a fine emulsion which is essential to rapid absorption when admixed with bile.

Effect of Posture on the Lungs.

W. H. WILSON (*Journal of Physiology*, October, 1927) has determined the effect of posture on the volume of the lungs, as indicated by measurements of the reserve air. Reserve air is the term applied to that volume of air which can be expelled at will from the lungs after the end of a normal respiration. Most authors give one thousand five hundred cubic centimetres as the volume of the reserve air. Wilson finds that the volume of reserve air varies with the posture of the body in a man of average vital capacity from a minimum of as little as two hundred and fifty cubic centimetres in the recumbent supine, to a maximum of one thousand five hundred and fifty cubic centimetres in the erect position. Skiagrams of the thorax were also taken showing the level of the diaphragm under different conditions. These show a rise in the level of the diaphragm at the end of normal expiration of 1·25 centimetres (half an inch) in passing from the erect standing position to the erect easy and a further 2·5 centimetres (one inch) in passing to the recumbent posture. The observation of Haldane, Meakins and Priestley that the mixed arterial blood leaving the lungs is less fully saturated with oxygen than it would be if the amount of air breathed were evenly distributed over the alveoli, an effect which is exaggerated by shallow breathing and still more exaggerated in the recumbent posture is evidently related to the reduction of reserve air in the cumbent posture, is evidently related so often observed in severe heart or lung disease is also related to this diminution of reserve air.

BIOLOGICAL CHEMISTRY.

The Distribution of Electrolytes in Intestinal Obstruction.

D. W. ATCHLEY AND E. M. BENEDICT (*The Journal of Biological Chemistry*, December, 1927) have investigated the distribution of electrolytes in intestinal obstruction. They have made partitions of the serum electrolytes in two laboratory animals and in one clinical case of intestinal obstruction. The authors point out that their work confirms the observations already made in this field by Gamble and Ross. The essential changes found during obstruction were: (i) decrease in the total base, (ii) decrease in chlorides, (iii) increase in carbonates, protein anions, sulphates and phosphates, (iv) dehydration as determined by serum protein percentage, hæmatocrit and hæmoglobin. Gamble and Ross found a striking increase in the undetermined acids of the plasma and thought that this increase must be in part due to an increase in organic acids. The authors have found no consistent change in undetermined acids and hold that there is no necessity for assuming changes in organic acid content. Analysis of the factors causing the disappearance of chlorides indicates that this change is due: (i) to loss of basic chlorides and hydrochloric acid by vomitus and (ii) to replacement of the base bound to chlorides by acids (phosphate and sulphate) retained because of renal insufficiency. The findings in experimental renal insufficiency make it doubtful that this change is brought about by actual loss of chlorides from the body. Although the authors were primarily interested in the chemical aspects of intestinal obstruction, they comment on one clinical feature. They point out that the limited nature of their data is apparent and that their suggestion requires confirmation. The most consistent and striking change between the first and second specimens of blood of their patient was the great dilution of the serum as indicated by protein percentage, hæmatocrit and hæmoglobin. This chemical change was coincident with a great clinical improvement and they are led to infer that a simple determination of serum protein percentage may be the best aid in following treatment.

Calcium and Glucose Tolerance in Diabetes Mellitus.

MAX WHISHNOFSKY (*The Journal of Laboratory and Clinical Medicine*, November, 1927) has studied the effect of calcium administration on glucose tolerance in *diabetes mellitus*. His investigations were carried out on six patients suffering from diabetes of varying degrees of severity. Each patient, after fasting for fourteen hours, received one hundred grammes of glucose. Four specimens of blood were taken; one immediately before ingestion and three at intervals of forty-five minutes, two hours and three hours after ingestion. The blood sugar was estimated by the Cramer-Gittelman method in which the blood is obtained by pricking the finger tip. During the three hour period the urine was collected and its glucose content determined. Two or three days later a similar procedure was carried out with the following modifications. Two blood specimens were taken from the fasting patient one-half hour apart. Immediately after the first had been removed an intravenous injection of one gramme of calcium chloride was given. The diet during the period of experimentation was unchanged. It was found that the blood sugar level in patients I, III and VI was not influenced by calcium ingestion. In patient II there was an increase from 253 to 338 milligrammes per hundred cubic centimetres of blood and in patient IV a decrease from 243 to 200. Examinations of the blood sugar curves showed that in some cases they are not so high when calcium is given as in the control; in others the reverse is true. The author concludes that calcium does not appreciably influence the curve. He points out that this finding is at variance with the work of previous investigators. Examination of the urine revealed that in three instances a diminished output of glucose occurred when calcium was given. The author hopes to continue the work by using parathyreoid extract.

The Multiple Nature of Vitamin B.

EVER since the term vitamin *B* was applied to the antineuritic accessory food factor and to the "water soluble *B* growth essential," various writers have uttered warnings against the acceptance of the indication of identity and have pointed out the possibility of two substances essential to nutrition being covered by the one designation. H. C. Sherman and J. H. Axtmayer (*The Journal of Biological Chemistry*, October, 1927) have made a quantitative study of this question. The foods used in their experiments were ground whole wheat, autoclaved yeast and dried, skimmed milk. The wheat was purchased whole, thoroughly freed from dust and other extraneous matter and ground in a mill used only for this purpose. Dried bakers' yeast was placed in uncovered Petri dishes to a depth of about fifteen millimetres and heated in an autoclave at a pressure of one atmosphere for 150 minutes. Then after being cooled and dried in the air, it was ground to a powder in a mortar. The dried, skimmed milk was used as obtained in the open market. These test foods were fed separately and in combination as sources of vitamin *B* to standard test animals on basal vitamin *B*-free diet. The object was to determine whether merely additive results or evidence of supplementary relationships would be found. The authors conclude from the resulting average weight curves that there was plainly a supplementary relationship and not merely an additive effect, when the wheat and yeast were fed together, as compared with the feeding of wheat separately, as the source of vitamin *B*. The authors hold that these experiments have yielded data which establish beyond any reasonable doubt the significance of the differences in growth and that these differences support the view that the vitamin *B* complex contains more than one substance essential to growth. They believe also that these data demonstrate the practicability of employing this method to determine which of the two recognized factors of this complex is the limiting factor in the vitamin *B* value of a given food and conversely whether the food is relatively richer in the other factor. Thus, the autoclave yeast which has been rendered poor in vitamin *F*, is found to be still a relatively rich source of vitamin *G*. Vitamin *F* is regarded as the antineuritic and vitamin *G* as the other and more thermostable factor. Vitamin *G* is found to be the limiting factor of the vitamin *B* complex of whole wheat which is therefore relatively richer in vitamin *F* than in vitamin *G*. Vitamin *F* is found to be the limiting factor of the vitamin *B* complex of milk, which is therefore relatively richer in vitamin *G* than in vitamin *F*. The authors hold that two new designations are desirable and that until truly chemical names can be assigned, it is better to adhere to the plan adopted by the majority of writers and to assign new letters in alphabetical sequence as the need for each becomes clear.

Cholesterolæmia and Deposits of Cholesterol in the Gall Bladder.

A HISTOLOGICAL study of the "strawberry gall bladder" as well as the evidence presented in recent literature suggests that the cholesterol found in the walls of gall bladders of this type is of a metabolic and not of an inflammatory origin. F. E. Blaisdell and L. R. Chandler (*The American Journal of the Medical Sciences*, October, 1927) have found cholesterol deposited in the human aorta, spleen and liver in three cases of strawberry gall bladder studied *post mortem*. They have carried out a series of experiments in order to determine if possible the relation between hypercholesterolæmia produced by feeding cholesterol and the deposits of cholesterol in certain characteristic cells in the mucosa and submucosa of the gall bladder. They have used fifteen rabbits and ten dogs for their experiments. They found that a hypercholesterolæmia was produced in all the animals by feeding cholesterol. A continued hypercholesterolæmia resulted in deposits of cholesterol containing fat in certain characteristic cells in the mucosa and submucosa of the gall bladder, when the cystic duct was patent. When the cystic duct was ligated before feeding cholesterol, the hypercholesterolæmia was produced, but no cholesterol-containing fat was found in the gall bladder wall, not even in the epithelium. They conclude that the deposits of cholesterol in the wall of the gall bladder are dependent on absorption of cholesterol from bile.

British Medical Association News.

SCIENTIFIC.

A MEETING OF THE SECTION OF NEUROLOGY AND PSYCHIATRY AND OF THE SECTION OF MEDICINE OF THE NEW SOUTH WALES BRANCH OF THE BRITISH MEDICAL ASSOCIATION was held at the B.M.A. Building, 30-34, Elizabeth Street, Sydney, on December 1, 1927, DR. S. A. SMITH, President of the Branch, in the chair.

Vascular Disturbances and Nervous Symptoms.

PROFESSOR A. E. MILLS read a paper entitled "Vascular Disturbances as an Explanation of Nervous Symptoms" (see page 176).

DR. A. W. CAMPBELL congratulated the speaker on his paper. He thought that the importance of venous back pressure and œdema should be considered in addition to oxygen want as a cause of nervous symptoms. He remarked that in softening of the brain severe headache was an important symptom, but that the headache occurred only during the first few days of red softening. This might be due to oxygen want, but was more likely due to back pressure. With regard to epilepsy, Charcot had said that the cause of the fit was a spasm of cerebral vessels, but the convulsion occurred only when the brain had become congested. In migraine the initial phase was possibly a temporary spasm of a vessel. The fact that patients generally felt well before an attack came on, suggested that the headache might be due to subsequent congestion rather than a lack of blood supply to the brain.

PROFESSOR W. S. DAWSON discussed the paper from the point of view of psychiatry. He said that the thalamic overaction in cases of mania and melancholia might have a vascular basis. Many of the phenomena in *dementia præcox* might be due to vascular causes and indeed a primary vascular deficiency had been demonstrated in this condition.

DR. HARVEY SUTTON stated that he had been present at the incident described in Professor Mills's paper in regard to Professor Haldane's demonstration. He said that the colour of the subject had not been blue, but rather a livid tint which gradually became blue, and the only pain experienced by the subject had been during recovery which was accompanied by tingling sensations. There was no pain in carbon monoxide poisoning, nor in suffocation due to carbon monoxide in submarines. Anoxæmia, therefore, of itself was not necessarily painful in its general effects. When pain occurred in the gangrenous foot, might it not be an effect on the nerve fibre itself, as is seen in causalgia? The nerve endings modified stimuli into messages of sensation, the direct action on the nerve fibres meant a feeling of pain. Again, he would like to hear the explanation of headaches in children commonly caused by visual defect. When headache was due to refractive error in the eyes, the pain seemed to be outside the head. In gastric ulcer was not the referred pain most likely due to an irritation of the nerve endings? Dr. Harvey Sutton thought that the anoxæmia theory should get far more consideration than it had been given in the past and considered Professor Mills's paper had done much to draw our attention to its importance.

DR. H. C. MCDOUALL asked how the sensitivity of nerve endings was increased by lack of oxygen. He leaned to the congestion theory as to the cause of pain in migraine. Perhaps a poison might be produced which initiated the sequence of events in this complaint. It was hard to understand why there should be a spasm of a vessel and why this spasm would pass away without any obvious cause. He asked why the lack of oxygen caused pain in some cases and not in others.

DR. OLIVER LATHAM stated that he had examined cases of amputated painful limbs in which the arteries were so thickened, chiefly from fibrous overgrowth and transformation, that scarcely any lumen persisted. Sometimes it was not the larger vessel, but the arterioles and capillaries which were most affected. In these cases they became like minute rigid pipes and were commonly associated with an accompanying fine but generalized fibrous overgrowth and transformation, affecting all the tissues of the part. Both from pathological and clinical evidence arterial blood to the parts was diminished and intense pain was the chief symptom complained of, although trophic disturbances were evident also. Cases were quoted in which great pain in the limb and elsewhere and general misery had been relieved even for ten years by the amputation of the limb with the worst symptoms and this supported the theory that the pain was due to a diminished arterial blood supply.

DR. J. A. L. WALLACE stated that the persistence of pain caused by vascular engorgement, referred to by Professor Mills as possibly being due to the damage of tissue cells, might also appear aggravated by the "memory" of the first acutely painful sensation. At the Mental Hospital, Callan Park, there was a patient who had once been a medical student and was suffering from the effects of chronic morphinism. This man also had a duodenal ulcer. Even admitting the probable painful effects of the ulcer, Dr. Wallace considered that the craving for morphine exaggerated these painful sensations. The patient's symptoms were inconsistent with the demeanour of a man suffering the agonizing pains the patient described. He considered that the prolonged use of morphine caused an instability of the nerve cells, owing to which they are affected unduly by slight painful stimuli.

DR. EVAN JONES stated that the value of the paper was to help in the translation of all symptoms in terms of physiology. It was hard to understand why there should be pain where a specific stimulus was not present.

DR. C. G. MCDONALD mentioned a patient at the Royal Prince Alfred Hospital who had been under the care of Professor Mills. This patient knew when he was about to have a convulsion, owing to an epigastric aura. When lumbar puncture was performed and ninety cubic centimetres of fluid removed, the fit was averted and it was shown by examination of the urine that there was a congestion of the kidney at that time. He thought that when congestion occurred there must also be an oxygen want and anoxæmia of the nerve endings. When pain occurred in the bowel, the pain was due probably to anoxæmia of the nerve endings and not to mere stretching of the bowel.

DR. RALPH NOBLE mentioned how frequently it was possible to relieve a succession of epileptic fits by a lumbar puncture. The congestion of the brain in such cases was probably not the actual cause of the fits, but the congestion caused by an anoxæmia of the nerve cells. Professor Mills had given those present physiological principles and on these principles they might be able to base their treatment. For instance, in the treatment of epilepsy, they had always attempted to soothe the nerve cells with sedatives, but they had never attempted to prevent the constriction of vessels which was leading to the anoxæmia of the nerve cells.

DR. S. A. SMITH stated that he had never felt that the term "congestion" was satisfying, since it did not go far enough. Although familiar with Professor Mills's views on anoxæmia, he had never before heard the facts marshalled as they had been that evening and as a result he was more than ever convinced of the truth of Professor Mills's theory. The evidence relating to mountain sickness was exceptionally valuable, as it was almost like a laboratory experiment.

PROFESSOR MILLS in reply said that he felt the criticism had been too kind and gentle. Dr. Campbell had instanced red softening as evidence of irritation causing nervous symptoms, but the same argument might be used for anoxæmia. In the zone of œdema there would be interference with the transfer of oxygen to the tissues and this interference would occur whether there were congestion or œdema. Pain was the expression of a dynamic condition due to hypersensitiveness of nerve cells. In anoxæmia nerve cells were sensitive to stimuli which under ordinary conditions would not lead to response. The time factor in congestion of the brain was important. The pain due to eye strain, mentioned by Dr. Harvey Sutton, was referred to the periphery. The theory of congestion was only a midway house to the theory of deprivation of oxygen as a cause of nervous symptoms. There was no explanation of pain, just as there was no explanation of life, but the facts seemed to show that pain arising from nerve cells was due to anoxæmia of those cells.

NOMINATIONS AND ELECTIONS.

THE undermentioned have been nominated for election as members of the New South Wales Branch of the British Medical Association:

Holt, Walter Gerald, M.B., B.S., 1927 (Univ. Sydney), 3, Tusculum Street, Potts Point.
Phillips, John Richard, M.B., Ch.M., 1925 (Univ. Sydney), Glebe Street, Ryde.
Ducker, Alan Lyall, M.B., B.S., 1927 (Univ. Sydney), Royal North Shore Hospital, St. Leonards.
Spedding, Ronald Louis, M.B., 1926 (Univ. Sydney), 9, Cowper Street, Randwick.

THE undermentioned have been elected members of the Victorian Branch of the British Medical Association:

Phillips, Henry Anthony, M.B., B.S., 1927 (Univ. Melbourne), Alfred Hospital.
Osborn, Gladstone Rule, M.B., B.S., 1927 (Univ. Melbourne), Melbourne Hospital.
Hadley, Robert Henry, M.B., B.S., 1927 (Univ. Melbourne), Melbourne Hospital.

Post-Graduate Work.

LECTURES AT LAUNCESTON.

A SERIES of post-graduate lectures and demonstrations was given at the Launceston Public Hospital, Tasmania, from January 21 to 24, 1928, by Dr. S. V. Sewell, Honorary Physician to In-Patients, Melbourne Hospital, and Mr. Alan Newton, Honorary Surgeon to In-Patients, Melbourne Hospital. The course was held under the auspices of the Northern Division of the Tasmanian Branch of the British Medical Association.

Renal Function.

Dr. Sewell lectured on tests of renal function. He pointed out that the whole kidney did not function at once, but that different parts came into action at different moments. Consequently there was a large reserve. As a result of this the function tests yielded positive results only when a large part of the kidney had been destroyed.

He then reviewed the theories of glomerular filtration and gave a summary of the normal functions of the kidney.

The tests for renal efficiency were then discussed. He laid special stress on the dilution and concentration tests as reliable and easily carried out tests. As an instance of the latter, he described the case of a man who had been admitted to hospital with severe and recurring hæmatemesis. The man had been operated upon, but did not recover from the operation. At *post mortem* examination it had been discovered that he had had chronic nephritis. Dr. Sewell had then recollected that he had noticed before operation that the specific gravity of the urine on the patient's admission was 1020. He should have realized at the time that the patient had been subjected to a severe concentration test and that the specific gravity should have been 1035 or more.

Renal Disease.

Dr. Sewell also lectured on renal disease. He was in the habit of classifying renal diseases as belonging to the two arms of a V. One arm represented the renal predominance and the other arterial predominance. At the top of one arm was the contracted white kidney and of the other cases of essential hypertension. As the arms converged so the diseases became less frankly arterial or renal.

He discussed the various causes of albuminuria.

In connexion with the hydræmic type of chronic nephritis he reveiwed the theories of causation of œdema and applied them to methods of treatment.

Appendicitis.

Mr. Newton lectured on appendicitis. He first discussed the variations in the anatomy of the organ. In operating on acute appendicitis he always made a McBurney's incision. The advantage of this incision was that it was over the organ and that no small intestine was seen. He laid special stress on this latter point. If more room was needed upwards, the incision was extended up and the internal oblique and *transversus* were split higher up. If more room was needed downwards the internal oblique and *transversus* could be separated from the anterior sheath of the rectus below the level of the *linea semicircularis*.

After the removal of the appendix he emptied the pelvis with a pump and not with swabs. At the same time he separated any adhesions likely to result in intestinal obstruction.

He uttered a warning against too small an incision.

As regards after treatment he had no objection to morphine. The patient was put in Fowler's position and given saline solution by the rectum. The apparatus used for this latter was that first introduced by Dr. Ramsay, of Launceston.

He was getting tired of violent purges and rarely used anything stronger than an "Alophen" pill followed by "Eno's Salts." The tube was removed within two days and replaced by one of specially soft rubber. This one should not be removed too soon. "Luminal" and bromides were used as sedatives. In cases of retention it was necessary in women to be certain that there was no "retention with overflow." The most useful enema was one composed of milk and treacle.

He reviewed a series of 363 cases of acute appendicitis operated on at the Melbourne Hospital.

In cases of so-called chronic appendicitis he greatly deprecated the use of a lower abdominal incision. The incision made was an upper right paramedian retracting the rectus outwards. In this way the organs of the upper part of the abdomen, such as the gall bladder, stomach and duodenum could be explored. There was usually no difficulty in delivering the appendix. If there was, he had no hesitation in tearing through the peritoneum on the outer side of the caecum.

Alimentary Conditions.

In his second lecture Mr. Newton reviewed in detail his method of dealing with the various alimentary conditions. He discussed pouches of the œsophagus and diverticula of the duodenum and sigmoid, gastric and duodenal ulcer, gall stones and carcinoma of the pancreas.

Mr. Newton also gave a clinical demonstration on cases of rectal carcinoma and gall stones.

Operative Technique.

In the mortuary he then demonstrated his technique in various operations, including thyreoidectomy, cholecystectomy and appendicectomy.

Clinical Demonstrations.

Dr. Sewell gave a demonstration on medical cases. He reviewed the nervous mechanism of the bladder and discussed the management of various nervous diseases when the bladder was involved.

He then demonstrated the lesions in a *post mortem* specimen of syphilitic aortitis. Finally he demonstrated on a patient his method of localizing cerebral tumours.

OTO-RHINO-LARYNGOLOGY.

WE have been asked to announce that a post-graduate course in oto-rhino-laryngology will be held in the ear, nose and throat clinic of the l'Hôpital de Strasbourg under the auspices of the Faculty of Medicine of the University of Strasburg from July 2 to 14, 1928. The course will be given by Professor G. Canuyt. The programme will be published at a later date.

LECTURES IN MELBOURNE.

THE Melbourne Permanent Committee for Post-Graduate Work announces that arrangements have been made with Professor F. R. Fraser, of Saint Bartholomew's Hospital,

London, to deliver a series of special lectures in Melbourne at the end of July, 1928. The exact dates and the titles of the lectures will be announced in a subsequent issue.

Research.

SCIENCE SCHOLARSHIPS AND GRANTS.

THE SCIENCE COMMITTEE OF THE BRITISH MEDICAL ASSOCIATION has issued the following notice to which we desire to direct the attention of members. It will be remembered that arrangements have been made whereby the Federal Committee of the British Medical Association in Australia will act on behalf of the Council of the Association in connexion with the scholarships and grants in aid of scientific research.

Scholarships.

The Council of the British Medical Association is prepared to receive applications for research scholarships as follows:

An Ernest Hart Memorial Scholarship of the value of £200 *per annum*;

Three research scholarships, each of the value of £150 *per annum*.

These scholarships are given to candidates whom the Science Committee of the Association recommends as qualified to undertake research in any subject (including State medicine) relating to the causation, prevention or treatment of disease. Each scholarship is tenable for one year, commencing on October 1, 1928. A scholar may be reappointed for not more than two additional terms. A scholar is not necessarily required to devote the whole of his or her time to the work of research and may hold a junior appointment at a university medical school or hospital, provided the duties of such appointment do not interfere with his work as a scholar.

Grants.

The Council of the British Medical Association is also prepared to receive applications for grants for the assistance of research into the causation, treatment or prevention of disease. Preference will be given, other things being equal, to members of the medical profession and to applicants who propose as subjects of investigation problems directly related to practical medicine.

Conditions of Award: Applications.

A copy of the regulations relative to the award of the scholarships and grants in 1928 and of the prescribed application form can be obtained on application to Dr. R. H. Todd, Secretary of the Federal Committee of the British Medical Association in Australia, B.M.A. Building, 30 to 34, Elizabeth Street, Sydney. The completed application form is required to be submitted to Dr. R. H. Todd not later than March 24, 1928. Applicants are required to furnish the names of three referees who are competent to speak as to their capacity for the research contemplated, to whom reference may be made.

ALFRED COX,
Medical Secretary.

British Medical Association House,
Tavistock Square, London, W.C.1.
November, 1927.

Correspondence.

WORKERS' COMPENSATION ACT.

SIR: Many of us were very glad to see Dr. Allen's letter *re* the sins of insurance companies. There is not the slightest doubt in my mind that on the whole these bodies are most unsatisfactory people with whom to deal. It is a very occasional general practitioner who cannot tell of accounts returned to him by one or other of the insurance companies, accompanied by an insulting letter to the effect that he is grossly overcharging. One is glad to see that a few practitioners are taking a very firm stand in this matter and are refusing to reduce their accounts one penny piece. If every medical man acted in a similar way our lot would be a much happier one.

Another very unsatisfactory action of these insurance companies is their effort to compel all injured workers to see the company doctor once a week. It ought to be realized by every practitioner and every worker that the companies have not the slightest power to enforce this "order." The Act distinctly says that the patient may be seen by the employer's (*id est* the insurance company's) medical representative only by arrangement with and in the presence of the patient's own doctor. There should be a notice to that effect pasted up in every workshop. Many patients are informed that they will not be able to draw their compensation unless they report to the insurance company's doctor each week. Four of my patients have been told that within the last few weeks. I instructed them all to ignore the company. After a little argument their monies were paid to them. Every medical man should point blank refuse to allow his patients to go unattended to insurance companies' medical men. They have no standing whatsoever under the Act and are an excrescence on the insurance system. Any disputes between the patient's doctor and the company can very well be decided by the medical referees of the Workers' Compensation Commission.

I feel very strongly on this subject. Recently after attending a man suffering from an ulcerating leg for four months, I sent his employer's insurance company a bill for twenty guineas. They replied offering me five pounds ten shillings. I demanded that the case be taken before the Commission and, instead of so doing, I received my cheque for twenty guineas the same week. Another lad with a cut hand was treated by me for three weeks and his account for five guineas was dispatched in due course to another company. They replied by offering me two. A similar demand for Commission investigation brought a hurried five guinea cheque next mail. One could go on quoting these cases *ad infinitum*.

I think it is time that medical men took a firm stand with this class of creditor. I suggest to begin with that our Association's New South Wales Branch ask the Workers' Compensation Commission to order the prominent display in every workshop of a copy of the *Workers' Compensation Act* and all amendments thereto.

Yours, etc.,

G.P.

January 30, 1928.

RED-BACKED SPIDER BITE.

SIR: I recently had a case of a child, aged five years, who had been bitten by a red-backed spider which presented features I have not previously come in contact with. I can find no reference to the condition in any books at my disposal, so am asking you to publish this as I would be glad to know if others have had similar cases and what line of treatment has proved effective.

At 7 p.m. on December 27, H.C., *ætatis* five years, was bitten on the hand; about fifteen minutes later a ligature was applied above the wrist and the wound scarified and rubbed with potassium permanganate crystals. The child was then put in a car and brought into town, a distance of one hundred miles, and on the way she complained first of pain in the whole of the affected arm and later in both legs. An hour before reaching town the tourniquet was loosened and then reapplied very loosely. When I saw the child, about six hours after being bitten, she felt well and made no complaint of any pain or abnormality. She was admitted to hospital for observation and at 11 a.m. the hand and the left side of her face were swollen. She had a temperature of 99·4° F. and was sweating freely. She was put on a diaphoretic mixture and in the evening her temperature had risen to 100·4° F. She continued to sweat freely for the succeeding nine days. On December

29, the right half of the upper hip commenced to swell. She was put on calcium lactate, five grains thrice daily. At 9 p.m. she lost her power of speech and swallowing for a few minutes.

The right cheek and upper lip now became swollen and the left side subsided; temperature 101·2° F.

On January 1 she developed a profuse irritable rash on the body and limbs and face and the temperature remained at 101° F. The rash subsided in four days and the temperature gradually fell to normal by January 8.

I have seen several other cases of spider bite recently, all of which showed as the main symptom severe pain in the part bitten and none has shown swellings, rash or sweating, while morphia was required to relieve the pain.

Yours, etc.,

G. M. B. HALES.

Brewarrina, New South Wales.
January 18, 1928.

PRESS NOTICES.

SIR: Old fashioned by upbringing, education and sentiment, yet with enough of the *joie de vivre* existent to realize we must move with the times, I am stunned when I, waiting for elusive patients, pick up my copies of the daily press and read accounts of the doings, social successes and academic flights of members of our profession, which accounts are further embellished with pleasing photographs of the heroes. I say I am stunned because such was not the case in days of yore and I cannot comprehend the *raison d'être*, if such there be. Is it a counterblast to a prophet is not known in his own country; is it an ebullition of enthusiasm on the part of an adoring aunt; is it a way of reaching the steely hearts of directors who may have a problematical job in their pockets and must not be personally canvassed; or is it that our press is becoming yellow?

Our legal brethren take trips across the Tasman or to the Caves which are duly chronicled, the reason being, so our legal wag informed me, "our landlords always know our *locus standi*," but this does not apply to our profession as we (?) wealthy citizens all own our own lairs.

The more one writes, the more one thinks, the more one puzzles and I am sure it is not done for the ulterior motives which have been ascribed.

Can you enlighten us, Sir, or are you stunned?

Yours, etc.,

SIDERE MENS EADEM MUTATO.

January 30, 1928.

POST-GRADUATE WORK IN PARIS.

SIR: May I point out for the benefit of Australian medical men visiting Europe that there exists in Paris an "*Association pour le Développement des Rélations Médicales entre la France et les Pays Alliés ou Amis.*"

This association has its bureau at the Salle Béclard, in the Faculté de Médecine, Rue de l'École de Médecine, Paris, and there the visiting medical man or student will find a welcome and can obtain any information about hospitals, clinical demonstrations, operating days and so forth. The practice of the hospitals is free, but for the special post-graduate courses held from time to time at the different hospitals a trifling charge is made. Professor Hartmann is president of the "A.D.R.M." (as the association is commonly known) and his name is a sufficient guarantee of its standing and efficiency.

In a recent number of *La Presse Médicale* (November 26, 1927) it was announced that during the preceding few months 613 visiting medical men had been enrolled at the Salle Béclard, of whom seventy-six were from the United States of America and twenty-two from England, but none, I fear, from New Zealand or Australia.

I feel it my duty to say how excellent is the clinical material available, how refreshing the different viewpoint on many medical matters, how arresting the scientific and experimental work being done there.

It should surely be the aim of us all to strengthen the bonds of friendship with our colleagues of a country with whom but recently we stood shoulder to shoulder in the greatest crisis of our times.

It is the fervent wish of one who acknowledges his indebtedness to his French *confrères*, that the Australian doctor of the future will pierce beyond the boulevards of the cosmopolitan city and see the real heart of France beating in clinic and laboratory.

Yours, etc.,

235, Macquarie Street, Sydney. H. M. MORAN.
January 15, 1928.

Proceedings of the Australian Medical Boards.

VICTORIA.

THE undermentioned have been registered under the provisions of Part I of the *Medical Act* 1915, of Victoria, as duly qualified medical practitioners:

Barnett, Harry, M.B., Ch.M., 1923 (Univ. Sydney), 125, Victoria Street, Ballarat East.

Milazzo, Guiseppe, M.D., Ch.M., 1915 (Catania, Italy), 15, Drummond Street, Carlton.

Sarzano, Luigi, M.D., Ch.D., 1911 (Modena, Italy), Milton House, 25, Flinders Lane, Melbourne.

Additional diploma registered:

Simpson, George, M.R.C.P. (London), 1926.

Medical Appointments.

Dr. Alexander Tennant Chapple (B.M.A.) has been appointed Government Medical Officer at Lithgow, New South Wales.

* * * *

Dr. Malcolm Leslie Scott (B.M.A.) has been appointed Honorary Surgeon at the Adelaide Hospital, South Australia.

* * * *

Dr. Philip Santo Messent (B.M.A.) has been appointed Honorary Assistant Surgeon at the Adelaide Hospital, South Australia.

* * * *

Dr. William Archibald Jock Nairne has been appointed a Resident Medical Officer at the Adelaide Hospital, South Australia.

* * * *

Dr. Malcolm August Trudinger has been appointed an Acting Resident Medical Officer at the Adelaide Hospital, South Australia.

* * * *

Dr. Hugh McIntyre Birch (B.M.A.) has been appointed Acting Deputy Superintendent of the Parkside Mental Hospital, South Australia.

Books Received.

A TEXT-BOOK OF INFECTIOUS DISEASES, by E. W. Goodall, O.B.E., M.D., B.S. (London); Revised and in large part re-written; 1928. H. K. Lewis and Company, Limited. Demy 8vo., pp. 734, with illustrations. Price: 30s. net.

CLINICAL HANDBOOK FOR RESIDENTS, NURSES AND STUDENTS, Edited by Victor M. Coppleson, M.B., Ch.M., F.R.C.S., 1928. Sydney: Angus and Robertson, Limited. Crown 8vo., pp. 153.

ULTRA-VIOLET RAYS IN THE TREATMENT AND CURE OF DISEASE, by Percy Hall, M.R.C.S. (England), L.R.C.P. (London), with Introductions by Sir Henry Gauvain, M.A., M.D., M.C. (Cambridge), F.R.C.S., and Leonard E. Hill, M.B. (London), F.R.S.; Third Edition; 1927. London: William Heinemann (Medical Books) Limited. Demy 8vo., pp. 254, with illustrations. Price: 12s. 6d. net.

DISEASES OF THE THROAT, NOSE AND EAR, by Dan McKenzie, M.D., F.R.C.S.E.; Second Edition; 1927. London: William Heinemann (Medical Books) Limited. Imp. 8vo., pp. 688, with illustrations. Price: 45s. net.

THE PRINCIPLES OF ANTE-NATAL AND POST-NATAL CHILD HYGIENE, by W. M. Feldman, M.D., B.S., M.R.C.P. (London), F.R.S. (Edinburgh); 1927. London: John Bale, Sons and Danielsson, Limited. Royal 8vo., pp. 765, with illustrations. Price: 25s. net.

A TEXT-BOOK OF MEDICINE, by American Authors; Edited by Russell L. Cecil, A.B., M.D.; Associate Editor for Diseases of the Nervous System, Foster Kennedy, M.D., F.R.S.E.; 1927. Philadelphia: W. B. Saunders Company; Melbourne: James Little. Royal 8vo., pp. 1522, with illustrations. Price: 45s. net.

DIAGNOSIS AND TREATMENT OF DISEASES OF THE STOMACH WITH AN INTRODUCTION TO PRACTICAL GASTRO-ENTEROLOGY, by Martin E. Rehfuss, M.D.; 1927. Philadelphia: W. B. Saunders Company; Melbourne: James Little. Royal 8vo., pp. 1236, with illustrations. Price: 66s. net.

HEALTH SUPERVISION AND MEDICAL INSPECTION OF SCHOOLS, by Thomas D. Wood, A.M., M.D., and Hugh Grant Rowell, A.B., M.D.; 1927. Philadelphia: W. B. Saunders Company. Melbourne: James Little. Royal 8vo., pp. 637. Price: 37s. 6d. net.

TEXT-BOOK OF BACTERIOLOGY, by William W. Ford, M.D.; 1927. Philadelphia: W. B. Saunders Company; Melbourne: James Little. Royal 8vo., pp. 1069, with illustrations. Price: 42s. 6d. net.

STUDIES IN PSYCHOLOGY, by William Elder, M.D., F.R.C.P.E., F.R.S.E.; 1927. London: William Heinemann (Medical Books) Limited. Demy 8vo., pp. 226. Price: 8s. 6d. net.

TOBACCO AND PHYSICAL EFFICIENCY: A DIGEST OF CLINICAL DATA, by Pierre Schrumpf-Pierron, M.D.; 1927. New York: Paul B. Hoeber, Incorporated. Demy 8vo., pp. 147. Price: $1.85 net.

NASAL NEUROLOGY, HEADACHES AND EYE DISORDERS, by Greenfield Sluder, M.D., F.A.C.S.; 1927. St. Louis: The C. V. Mosby Company; Melbourne: Stirling and Company. Royal 8vo., pp. 428, with illustrations. Price: $11.50 net.

DISEASES OF THE MOUTH, by Sterling V. Mead, D.D.S.; 1927. St. Louis: The C. V. Mosby Company; Melbourne: Stirling and Company. Royal 8vo., pp. 578, with illustrations. Price: $10.00 net.

THE NORMAL DIET, by W. D. Sansum, M.S., M.D., F.A.C.P.; Second Edition; 1927. St. Louis: The C. V. Mosby Company; Melbourne: Stirling and Company. Post 8vo., pp. 166. Price: $1.50 net.

DISEASES OF THE SKIN, by Henry H. Hazen, A.M., M.D.; Third Edition; 1927. St. Louis: The C. V. Mosby Company; Melbourne: Stirling and Company. Royal 8vo., pp. 572, with illustrations. Price: $10.00 net.

THE PRACTICAL MEDICINE SERIES, COMPRISING EIGHT VOLUMES ON THE YEAR'S PROGRESS IN MEDICINE AND SURGERY: Under the General Editorial Charge of Charles L. Mix, A.M., M.D.; General Medicine; 1927. Chicago: The Year Book Publishers. Crown 8vo., pp. 761, with illustrations. Price: $3.00 net.

ANNALS OF THE PICKETT-THOMSON RESEARCH LABORATORY, Volume III.; 1927. London: Baillière, Tindall and Cox. Demy 4to., pp. 320, with illustrations. Price: 42s. net.

PRACTICAL BIRTH CONTROL: BEING A REVISED VERSION OF SAFE MARRIAGE, by Ettie A. Hornibrook, with Preface by Sir William Arbuthnot Lane, Bart, C.B., M.S.; Sixth Impression; 1927. London: William Heinemann (Medical Books), Limited. Crown 8vo., pp. 53. Price: 3s. 6d. net.

Diary for the Month.

FEB. 14.—Tasmanian Branch, B.M.A.: Branch.
FEB. 14.—New South Wales Branch, B.M.A.: Ethics Committee.
FEB. 20.—New South Wales Branch, B.M.A.: Organization and Science Committee.
FEB. 21.—Tasmanian Branch, B.M.A.: Council.
FEB. 21.—New South Wales Branch, B.M.A.: Executive and Finance Committee.
FEB. 22.—Victorian Branch, B.M.A.: Council.
FEB. 24.—Queensland Branch, B.M.A.: Council.
FEB. 28.—New South Wales Branch, B.M.A.: Medical Politics Committee.
MAR. 2.—Queensland Branch, B.M.A.: Branch.

Medical Appointments Vacant, etc.

For announcements of medical appointments vacant, assistants, *locum tenentes* sought, etc., see "Advertiser," page xviii..

COMMONWEALTH DEPARTMENT OF HEALTH: Medical Officer.
THE BRISBANE AND SOUTH COAST HOSPITALS BOARD: Assistant General Medical Superintendent.

Medical Appointments: Important Notice.

MEDICAL practitioners are requested not to apply for any appointment referred to in the following table, without having first communicated with the Honorary Secretary of the Branch named in the first column, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

BRANCH.	APPOINTMENTS.
NEW SOUTH WALES: Honorary Secretary, 30 - 34, Elizabeth Street, Sydney.	Australian Natives' Association. Ashfield and District Friendly Societies' Dispensary. Balmain United Friendly Societies' Dispensary. Friendly Society Lodges at Casino. Leichhardt and Petersham Dispensary. Manchester United Oddfellows' Medical Institute, Elizabeth Street, Sydney. Marrickville United Friendly Societies' Dispensary. North Sydney United Friendly Societies. People's Prudential Benefit Society. Phœnix Mutual Provident Society.
VICTORIAN: Honorary Secretary, Medical Society Hall, East Melbourne.	All Institutes or Medical Dispensaries. Australian Prudential Association Proprietary, Limited. Mutual National Provident Club. National Provident Association. Hospital or other appointments outside Victoria.
QUEENSLAND: Honorary Secretary, B.M.A. Building, Adelaide Street, Brisbane.	Members accepting appointments as medical officers of country hospitals in Queensland are advised to submit a copy of their agreement to the Council before signing. Brisbane United Friendly Society Institute. Stannary Hills Hospital.
SOUTH AUSTRALIAN: Secretary, 207, North Terrace, Adelaide.	All Contract Practice Appointments in South Australia. Booleroo Centre Medical Club.
WESTERN AUSTRALIAN: Honorary Secretary, 65, Saint George's Terrace, Perth.	All Contract Practice Appointments in Western Australia.
NEW ZEALAND (WELLINGTON DIVISION): Honorary Secretary, Wellington.	Friendly Society Lodges, Wellington, New Zealand.

Medical practitioners are requested not to apply for appointments to positions at the Hobart General Hospital, Tasmania, without first having communicated with the Editor of THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, New South Wales.

Editorial Notices.

MANUSCRIPTS forwarded to the office of this journal cannot under any circumstances be returned. Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary be stated.

All communications should be addressed to "The Editor," THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, Sydney. (Telephones: MW 2651-2.)

SUBSCRIPTION RATES.—Medical students and others not receiving THE MEDICAL JOURNAL OF AUSTRALIA in virtue of membership of the Branches of the British Medical Association in the Commonwealth can become subscribers to the journal by applying to the Manager or through the usual agents and booksellers. Subscriptions can commence at the beginning of any quarter and are renewable on December 31. The rates are £2 for Australia and £2 5s. abroad *per annum* payable in advance.